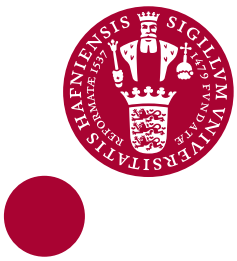

Lactation, milk and suckling

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Published in:
Nutritional physiology of pigs

Publication date:
2012

Document version
Publisher's PDF, also known as Version of record

Chapter 17
Lactation, milk and suckling

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This chapter deals with:

- An introduction to different aspects of sow lactation
- A description of hormonal and local regulation of mammary function
- An insight into the chemical composition of colostrum and sow milk
- A quantitative understanding of how dietary nutrients are utilized for milk production
- An insight into the importance of colostrum and milk for suckling piglets

1. Introduction

During the last 2-3 decades pig production has undergone changes with important consequences for the reproductive sow. Firstly, pigs are selected intensively for production of lean meat at slaughter, which has reduced the fat depots of both sows and suckling piglets, and secondly, pigs are selected for high litter size with amazing success. Since 1994, the average litter size in the Danish pig production has increased from 12 to 16 total born piglets per litter [64]. The lactation period is an important phase of the reproductive cycle, mainly because the sow has very high demands for nutrients to support milk synthesis, and because a high milk intake is crucial for survival and performance of piglets until weaning and even after. The genetic improvements of pig production during the recent decades have increased the metabolic load on the sow by increasing the amount of nutrients required to support the elevated milk production. Another consequence of successful breeding programmes is that the number of live born piglets often exceeds the number of functional mammary glands, and therefore cross-fostering is now widely used among Danish farmers.

Feeding and management of lactating sows is a challenging task. The reasons are mainly the lack of knowledge with regard to milk yield of the sow and how to improve it, because it is difficult to quantify the milk yield of sows. Much more knowledge on lactation is available for dairy cows, primarily because milk is the most important product in the dairy industry and because milk yield of dairy cows is easily recorded.

2. Onset, maintenance and termination of lactation

2.1. Onset of lactation

The onset of lactation can be divided into two stages: lactogenesis 1 and lactogenesis 2.

The mammary glands enter lactogenesis 1 approximately five weeks prior to farrowing. This stage may be detected by measureable amounts of colostral proteins in blood plasma. Colostrum production takes place in lactogenesis 1, whereas milk is not produced at that time as it is inhibited by high levels of plasma progesterone.

At farrowing, plasma progesterone decreases, thus the inhibition of milk synthesis is discontinued while increased plasma prolactin stimulates synthesis of milk components (e.g. a-lactalbumin, which is involved in synthesis of lactose) and mammary growth. These changes are probably the main driving forces for the mammary gland entering lactogenesis 2 characterized by the initiation of milk production. Other hormones such as oestrogen, oxytocin and relaxin are also involved [37], [23], [34], [35].

Piglet suckling is regarded as an additional driving force in order to onset lactogenesis 2 [34]. This would be in contrast to other species such as cows and humans where milk production is initiated regardless of whethere the glands are being milked or not. However, an experiment conducted at Aarhus University, Denmark, did not confirm the necessity of suckling for initiation of milk production (Theil et al., not published).

2.2. Maintenance of lactation

In lactogenesis 2, milk removal is necessary to maintain the milk production of individual mammary glands. If milk removal ceases (for instance if a piglet dies), the mammary gland quite rapidly undergoes involution. Involution is induced if milk stasis occurs for an extended period of time (less than one day). Milk production cannot be rescued in individual glands when the regression process has reached a “point of no return” which will occur after 40-60 hours of milk stasis [80]. However, during the next reproductive cycle all glands start to re-develop and they will again produce milk if suckled after parturition. Development of mammary glands and synthesis rate of milk are regulated at gland level by interactions between systemic factors such as circulating hormones and nutrient concentrations and local factors such as hormone receptors in the membrane of mammary epithelial cells. Right after milk removal, systemic factors, of which prolactin is the most important, are responsible for stimulating milk production (Figure 17.1A) and the rate of milk synthesis is high during the first 30-35 minutes after a suckling bout. As filling of the gland progresses, the synthesis rate of milk is inhibited by local factors (e.g. hormone receptors and transcription factors) that are controlled by milk stasis (Figure 17.1B). When the gland is emptied once again at the next suckling, the inhibition of milk synthesis due to milk stasis is relieved and milk synthesis resumes at maximum rate.

In contrast to the onset of lactation, maintenance of lactation seems only to be dependent on piglet suckling and plasma prolactin. Piglet suckling induces release of prolactin from the pituitary gland to the blood, and upon attachment to receptors in the mammary glands, prolactin elicits signals that stimulate milk production and mammary growth. The importance of prolactin for sow milk production was elegantly illustrated in a study by Farmer and co-workers, where sows were given bromocriptine to inhibit prolactin release. The sows responded by markedly reducing their milk yield, whereas their milk production increased again when the bromocriptine treatment ceased. However, prolactin is normally not the limiting factor for milk production, and improvement of sow milk yield using exogenous prolactin treatment has been tried without success. No other hormones are known to be involved directly in maintaining lactation. The hormone oxytocin is clearly necessary for milk letdown, but there is no existing knowledge about a direct role on maintaining milk synthesis. Growth hormone has a well described lactogenic effect in dairy cows, but growth

hormone administered to sows seems neither to influence milk yield nor to affect maintenance of lactation.

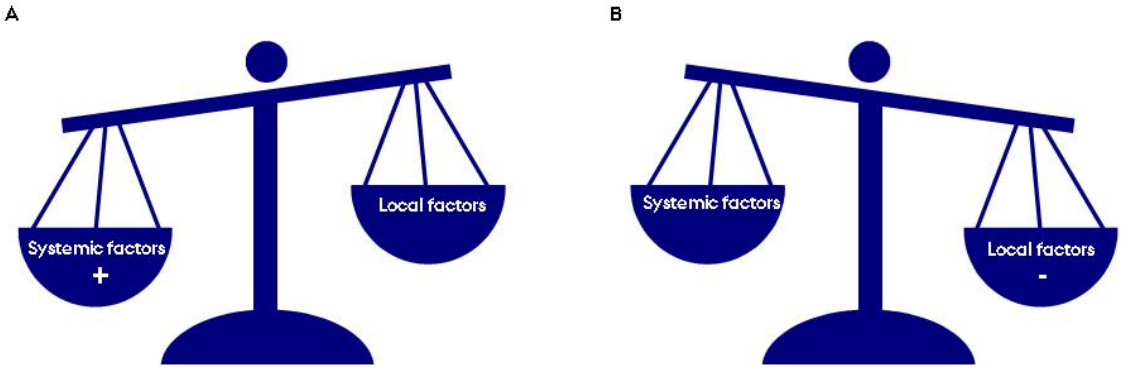


Figure 17.1. Rate of milk synthesis is regulated in concert by systemic factors such as circulating hormones and nutrient concentrations and local factors such as hormone receptors. After milk removal systemic factors stimulate the milk synthesis (A), but as the gland is being filled, local factors inhibit the rate of milk synthesis (B).

2.3. Termination of lactation

As previously mentioned, mammary glands begin to involute quite rapidly if they are not suckled. This occurs in early lactation for left-over glands when the piglets have developed a teat preference - but it also occurs at any time throughout lactation in individual glands if a piglet dies, and it occurs in all milk-producing glands right after weaning. There is no fundamental difference between involution in individual glands during lactation and that occurring in all active glands after weaning [40], [24]. If milk stasis remains in one or more glands for half a day, expression of prolactin receptors in the mammary gland will decrease, thereby uncoupling the stimulatory effects of prolactin on milk synthesis [81]. Furthermore, milk stasis will induce a mechanism that leads to programmed cell death (called apoptosis). Quite rapidly this will have severe consequences for the gland(s). If the milk stasis is relieved after 24 hours, the milk yield is reduced by approx. 25% throughout the lactation period, and if not relieved within approx. 50-60 hours, the gland has passed the “point of no return” and the gland will involute and become dry [80], [81].

3. Colostrum and milk – chemical composition

3.1. Changes in chemical composition during lactation

Colostrum is secreted at the day of farrowing (0-24 hours postpartum), and most colostrum is being ingested by piglets during the first 9-12 hours after birth [46] (Figure 17.2). In spite that colostrum is available only for a short period, the chemical composition changes quite dramatically (Table 17.1), likely because a minor amount of milk is being produced (which then dilutes the colostrum). The changing nature of the composition of mammary secretions (colostrum and milk) continues over the first 10 days of lactation. Major changes may occur during the first 3 days after parturition if sows are fed a high-fat diet, and the fat content of milk on days 2-3 may be doubled compared to the fat content of colostrum and mature sow milk [38]. Due to the transient changes of milk composition on days 2 and 3 postpartum, milk at this stage has been named transient milk.

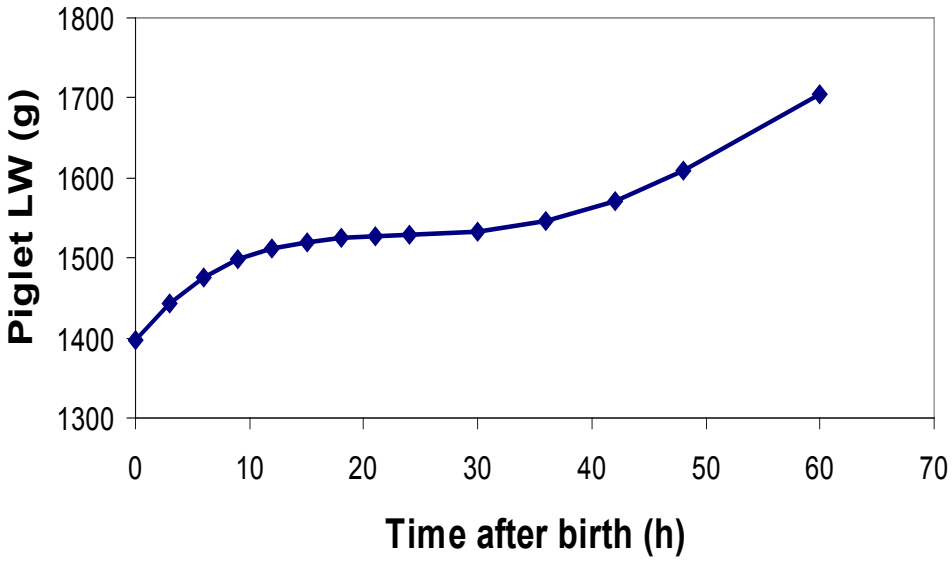


Figure 17.2. Changes in piglet weight (LW) during the first 2.5 days postpartum. The first 24 hours are regarded as the colostrum period, and the increase in piglet live weight around 32 hours after the first piglet is born marks the onset of lactation.

Sow milk on days 10-28 of lactation has a rather stable chemical composition and is referred to as mature milk. Mature milk contains 6-8% fat; 5.1-5.8% protein; 5.6 -5.8% lactose; 0.9% minerals; and a total of 18-20% solids (Table 17.1).

Table 17.1. Development of colostrum composition (0-24 hrs) and milk composition (days 2-28).

TIme after parturition[1]	Fat, %	Lactose, %	Protein, %	Total solids, %
0 h	5.2	3.4	16.3	-
3 h	5.9	3.4	15.2	-
6 h	5.8	3.3	13.1	-
9 h	6.0	3.8	10.8	-
12 h	6.6	3.8	9.9	-
24 h	7.9	4.4	9.4	-
2 d	6.5	4.8	6.4	18.6
3 d	6.7	5.2	6.1	19.0
7 d	6.7	5.6	5.4	18.3
14 d	6.4	5.9	5.1	18.2
21 d	6.6	5.8	5.2	18.7
28 d	6.1	5.8	5.4	18.1

1) Data obtained from [38] (0-24 hours postpartum) and [43] (2-28 days postpartum).

3.2. Dietary factors affecting milk composition

Several factors influence the chemical composition of sow milk: The dietary composition and the feeding level (energy intake) can directly affect the milk composition (Figure 17.3) by altering the supply of substrates used for synthesis of components in the milk (section 5). Lactose is the most stable fraction because it is the major osmotic factor in sow milk and thus responsible for drawing water into the milk. The contents of protein and minerals in milk are also rather constant as long as the dietary nutrient intake of the sows follows the recommendations or the sow is able to counter-balance improper nutrient intake by body mobilization. Without any doubt, the fat proportion of sow milk is the most variable fraction, and supplementation of dietary fat to sows has been investigated as a strategic tool to increase milk fat content and thereby litter performance.

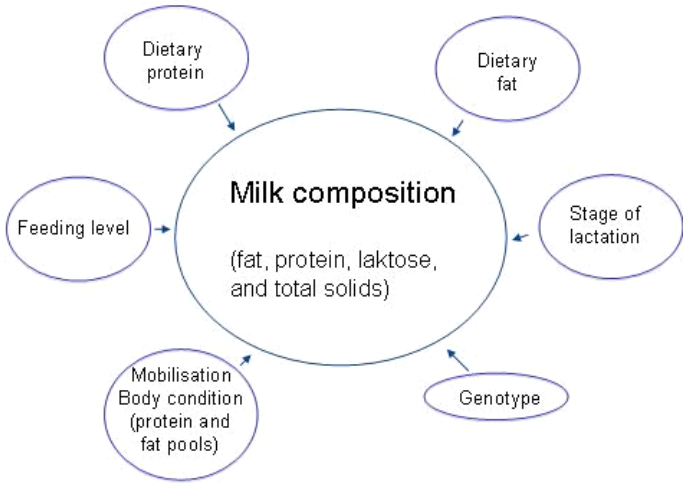


Figure 17.3. Factors related to the sow and to feed and feeding on chemical composition of sow milk.

Dietary protein: The protein content of sow milk can barely exceed 30% when expressed on a dry matter basis (equivalent to approx. 6.0% in mature milk). However, if the dietary supply of protein (or essential amino acids) is reduced 25-50% below the recommended level (due to low feed intake or imbalanced diets), the milk protein content or the total milk yield will be depressed. Depression of milk protein content or milk yield due to inadequate protein supply seems not to affect the amino acid profile of sow milk.

Dietary fat: Beneficial effects of supplementing dietary fat have been demonstrated on milk yield of sows. Most of the studies carried out were done with fat levels within 7.5-15% of dietary fat on a dry matter basis. Some studies found no beneficial effect of the fat (reviewed by [67]) but many studies report an increase in milk yield amounting to +8 to +15% among sows fed high-fat diets compared to control diets (containing 3-5% dietary fat). Most studies evaluated factors such as the duration of supplementing diets with additional fat and amount of dietary fat added, whereas only a few studies focused on the influence of adding fat of varying fatty acid composition. Dietary fat is included in lactation diets typically to improve the negative energy balance of lactating sows (i.e. less mobilization of nutrients from body pools) or to improve the milk fat output. However, it is important to stress that fat should not just be regarded as an energy source. A previous study carried out at AU, Denmark documented that some – but not all - dietary fat sources improved either the milk yield or the milk fat content [50]. Thus, beneficial effects depended on the fat source (animal fat, rapeseed oil, fish oil, coconut oil, palm oil, or sunflower oil), and in that study supplementation of dietary fat at 8% level improved the performance of the progeny by increasing the content of fat and energy of the sow milk. The study furthermore demonstrated that the fatty acid composition of the sow milk fat was highly variable, but in general, fatty acids abundant in the diets were also abundant in the milk fat.

Dietary fibres: A few studies have shown that a high intake of dietary fibre during lactation is associated with elevated levels of milk fat, but it is unclear whether this is a direct effect of higher levels of SCFA in plasma (section 5) or whether it is an indirect effect and merely a consequence of a higher mobilization due to a lower intake of metabolizable energy.

Dietary energy: Sows are able to support a high milk yield by body mobilization without greatly compromising the milk composition. If sows have a low appetite, they will mobilize nutrients from body pools of fat and proteins and utilize these nutrients for milk production. Mobilization of nutrients occurs in most sows during lactation because nutrients derived from the feed are insufficient to meet the demands for a high milk production. Sows that have a great mobilization produce milk with a higher fat content [88] and with a fatty acid composition reflecting that of body fat. This may be an effect of higher circulating levels of free fatty acids in the sows' plasma, which is then transferred across the mammary epithelium and becomes available for milk fat synthesis.

3.3. Bioactive components and roles of nutrients for the offspring

Colostrum has a higher content of various bioactive components when compared to mature sow milk. The most well-known are immunoglobulins A, G and M, which are important for the passive immune defense, and for piglet survival. However, colostrum also contains a variety of growth factors (e.g. Insulin-like growth factors I and II, Epidermal growth factor and Transforming growth factor -b), vitamins, minerals, peptide and steroid hormones, digestion enzymes (lipase, amylase and protease) and metabolites (glucose, galactose and fructose). The digestion enzymes are likely important for the newborn piglet to utilize the nutrients in ingested colostrum/milk, and the growth factors are important to ensure proper growth and development of organs, as growth of the gastro-intestinal tract is massive for newborn piglets during their first days of life [74].

Among the macrochemical components, lactose may be regarded as a fuel, whereas amino acids may be regarded as building blocks for protein synthesis (muscle and other tissues). Fat plays a different role in colostrum and in milk. In colostrum, energy supply to neonatal piglets is scarce and colostral fat is likely rather important as a fuel in this period to avoid neonatal death. In line with that assumption, colostrum contains lipase, which is necessary for fat digestion in the gut of newborn piglets. In contrast, fat in mature milk is mainly used for fat accretion, whereas lactose is the major substrate for oxidation.

4. Colostrum yield

The importance of sow nutrition on colostrum yield of sows is sparsely investigated [21]. Without any doubt, the lack of knowledge is related to the difficulties in collecting these data. In a recent study, the effect of nutrition during gestation and during the transition from gestation to lactation on colostrum yield was studied. During gestation, high-fibre diets (low in starch) were compared with a control diet with a low content of fibre (and high starch). No detrimental effects on colostrum yield and composition were observed even though the high-fibre diets contained up to 40% non-starch polysaccharides (Theil et al., unpublished). In the last week prior to parturition, sows were fed lactation diets supplemented with different fat sources (8% added fat). Sows fed a diet containing 8% coconut oil, 8% sunflower oil or 4% fish oil and 4% octanoic acid had a higher colostrum yield than sows fed a standard diet or a diet with 8% fish oil [31]. Colostrum yield was evaluated based on the piglet gain from birth until 24 hours after birth of the first piglet, and the improved performances of sows and piglets were associated with lower piglet mortality during the colostrum period. In a follow- up study, the effect of dietary CLA (trans-10, cis-12 conjugated linoleic acid) was studied. In contrast to expectations, the tested isomer of CLA inhibited the colostrum yield and consequently more piglets died or were cross-fostered to other sows during the first week of lactation [46].

5. Milk yield

A sow has a potential to produce milk, which to a great extent is determined by the genetic background. At peak lactation, the best-performing sows produce around 1.1 kg milk per piglet per day, which corresponds to max. 15 kg of milk for sows nursing large litters. During a 28-day lactation period, sows produce around 350 kg. These figures are estimates and based on relatively few experimental data, because direct measurements of milk yield of sows are expensive to obtain. Three different methods are used to estimate the milk yield of sows:1) regular recordings of piglet weight gain; 2) recordings of piglet weight before and after a suckling (weigh-suckle-weigh); and 3) measurements of milk water intake based on the deuterium oxide dilution technique. The estimation based on regular recordings of piglet weight is most commonly applied, but also the method with

lowest precision and accuracy. The most precise and accurate method is based on the deuterium oxide dilution technique [82].

The most important factors affecting mammary nutrient uptake, milk synthesis, and hence milk yield of sows, are discussed below. The data presented for mammary nutrient metabolism, estimated milk yields and piglet growth rates cannot be compared between experiments, because of different experimental approaches and numerous conditions affecting these data – but the data can be used to obtain an impression of the importance of the different factors affecting milk synthesis and milk yield in the sow mammary gland. It is also important to realize that many of these factors interact, which makes it difficult to compare milk yields between various experiments. For instance, the milk yield interacts with feed intake, mobilization of nutrients, body condition, and parity of the sow.

5.1. Parity

Milk production increases with parity (Table 17.2), and the largest difference is found when comparing gilts with sows of 2nd parity (Table 17.2). This difference is likely explained by different strategies for nutrient partitioning. Indeed, gilts have to prioritise their nutrients between own growth (which increases future reproductive output) and milk yield (which increases current reproductive output), whereas the milk yield is the top priority for older sows (parity ≥ 2). Older sows typically lose 20-30 kg during lactation, whereas gilts typically increase their body weight slightly during their first lactation illustrating how differently nutrients are partitioned in gilts and older sows. Some scientists have speculated that the higher milk yield observed in older sows compared to gilts was due to a higher feed intake because the gastric capacity is lower in gilts. Others have argued that a lower birth weight of piglets from gilts and thus a lower capacity to suckle the milk explains why gilts produce less milk than older sows. It is at present unclear which mechanism(s) are responsible for the lower milk yield of gilts, but it is rather likely that altered nutrient partitioning is involved.

Table 17.2. Daily milk production of sows in parities 1, 2 and 4 fed according to recommended level (100%) during gestation and lactation[1]

	Parity 1	**Parity 2**	**Parity 4**
Milk yield (kg/day) of sows fed according to recommendations	6.14^{c}	7.11^{b}	7.90^{a}
	(n = 56)	(n = 84)	(n = 84)

1) Modified after [10]. A,b,c: letters within row with different superscripts are significantly different (P<0.05).

5.2. Stage of lactation

Milk yield increases with progress of lactation and typically peaks in the 3rd or 4th week of lactation. The pronounced increase in milk yield, especially during the first 10 days of lactation, is associated with a massive mammary growth occurring during this period (Figure 17.4). The milk yield is to a great extent determined by the number of mammary epithelial cells that produce and secrete milk into the lumen of alveoli. However, also the differentiation of mammary epithelial cells has an impact on milk yield during this period. Differentiation of mammary epithelial cells is not well documented in sow mammary tissue, but studies carried out on mammary tissues from lactating cows, rats and mice demonstrate that some lobules (physical structures in the mammary gland) produce milk, whereas others do not, and the fraction of lactating lobules may explain why increased differentiation of mammary epithelial cells has an impact on milk yield with progress of lactation.

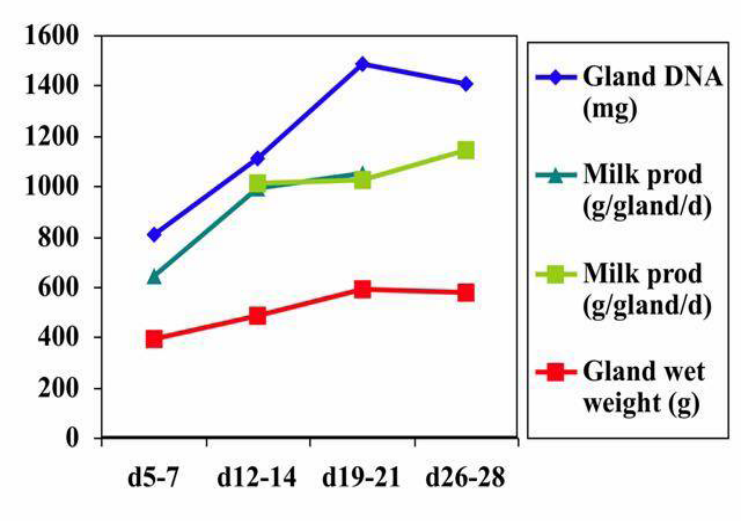


Figure 17.4. Changes in mammary gland size and milk yield during lactation.

A lactation curve has never been measured for sows throughout a lactation period. Based on the sparse amount of available data on milk yield of sows, different models (a Wood curve or a Gompertz function) can been fitted to mathematically describe the lactation curve of sows [39], [32] (Figure 17.5). Both mathematical models predict an increasing milk yield in early lactation and a peak either in week 3 (Wood curve) or in week 4 (Gompertz function). The total milk yield during a 28-day lactation period was predicted at 350 kg for both models, but the models do not fully agree on how fast the milk yield increases, when the milk yield peaks, or whether the yield declines or not in the fourth week of lactation. The discrepancy between the two models is likely caused by the limited number of experiments in which milk yield of sows was determined directly (i.e. by weigh-suckle-weigh or deuterium oxide dilution).

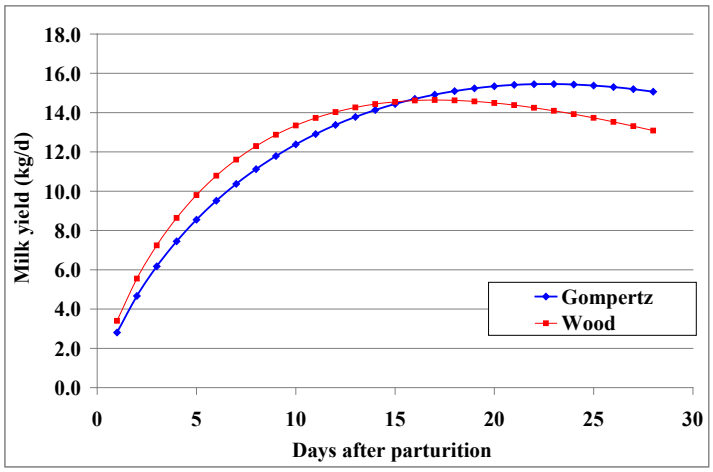


Figure 17.5. Mathematical description of the lactation curve of sows using a Gompertz or a Wood curve.

5.3. Litter size

The number of piglets has a profound positive effect on the milk yield, and the relationship between litter size and milk yield seems to be linear over quite a large range [3] (Figure 17.6a). The reason why litter size affects the milk yield is that each piglet suckles its own mammary gland. Thus, a large litter maintains a high number of lactating mammary glands. However, when expressed as milk production per gland per day (equivalent to milk ingested per piglet per day), the yield decreases with increasing litter size (Figure 17.6b), and the decreased milk yield per gland is higher in week 4 of lactation than in week 2.

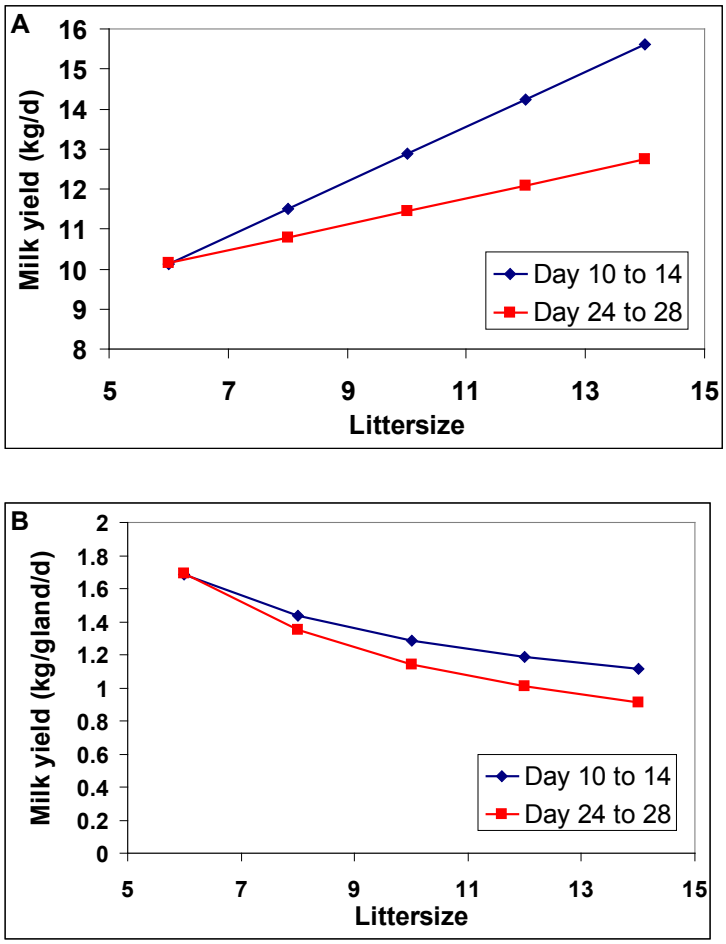


Figure 17.6. Effect of litter size on milk yield of gilts on days 10-14 and days 24-28 of lactation (modified from [3].

These findings suggest an upper limit on the nutrients that can be allocated for milk production. The lower milk yield per gland in the 4th week of lactation may indicate that the sow in this phase of the reproductive cycle begins to prioritize future offspring (the coming oestrus) higher than the current offspring (the milk yield). However, in week 4 of lactation the piglets also begin to ingest some dry feed, which may also explain why milk yield starts to drop.

5.4. Feed and feeding

Feed composition and feed intake of lactating sows are central factors for the performance of lactating sows. However, it is important to stress that lactating sows use the body pools of fat, protein (muscles) and glycogen as buffers to support the top-priority of nutrients (see Figure 17.7), and top-priority during early and mid-lactation is indeed production of milk.

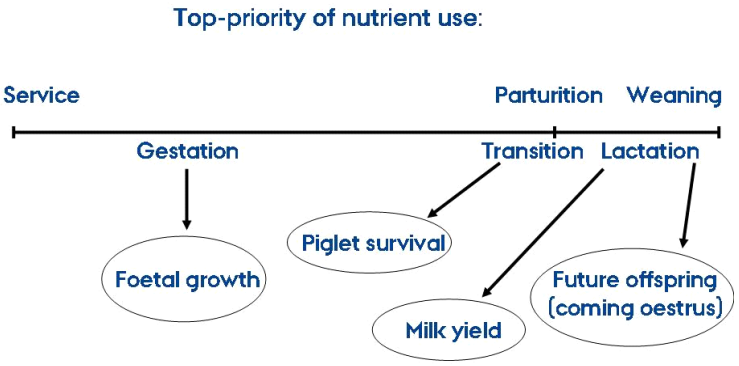


Figure 17.7. Top-priority of nutrient use in reproductive sows changes over the reproductive cycle.

Hence, the milk production is the most important trait for a sow like other lactating mammals, and therefore mobilization of nutrients should not be regarded a problem, but merely a must. The body of the sow may be regarded as a huge buffer of nutrients being mobilized to support the top-priority of nutrients if the dietary supply is a limiting factor (Figure 17.8). To give an overview of how feed and feeding affect the milk yield, it is necessary to distinguish between three categories: optimally fed sows, sub-optimally fed sows and malnourished sows that will be described separately below. It should be emphasized that the relationship between feed/feeding and milk yield differs between the three different categories of sows.

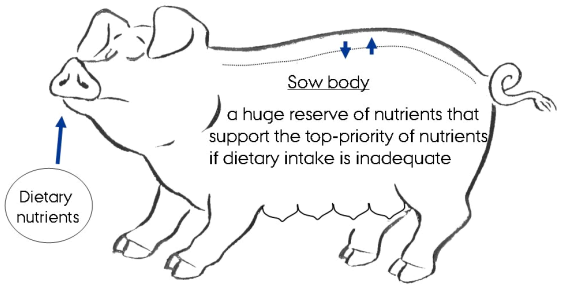
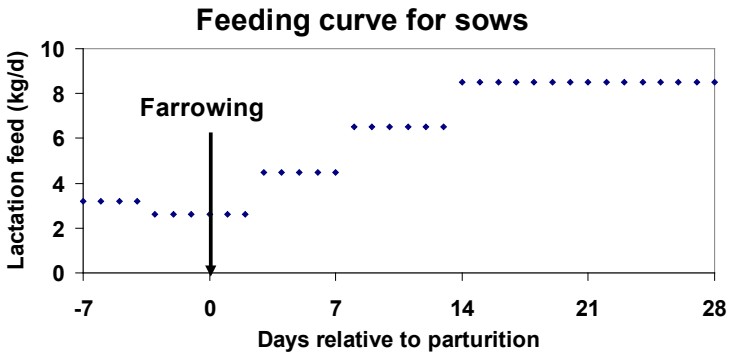


Figure 17.8. The sow body is a large reservoir of nutrients. Some of the pools of energy (fat) and amino acids (muscle tissue) are being mobilised during lactation to support the milk production.

Optimally fed sows: These sows are supplied a diet with recommended levels of dietary protein, essential amino acids, energy, vitamins and minerals (see Table 17.3), and feed intake (or feeding strategy) is adjusted according to body condition and production. During late gestation and early lactation, sows should be fed restrictedly, whereas sows should be fed close to ad libitum at peak lactation (Figure 17.9).

The milk yield of well-nourished sows is not limited by the feed intake or the feed composition. Nevertheless, the milk yield of these sows may be enhanced through feeding in several ways:

- 1) managing proper body condition at parturition (16-20 mm back fat),
- 2) supplementing a bioactive compound to enhance milk yield,
- 3) feeding sows closer to their requirement in late gestation and early lactation, or
- 4) affecting the mobilization of nutrients.



Figur 17.9. Recommended feed supply to sows during transition and lactation.

However, at present the third strategy is not applicable due to lack of knowledge of milk production, and the fourth strategy is not applicable due to lack of knowledge on how nutrient supply, nutrient mobilization and milk yield interact. It is a widespread misconception that the milk yield in general is limited by the feed intake of well-nourished sows. In an experiment where gilts were fitted surgically with a gastric cannula and fed 38% of feed in excess of ad libitum feed intake, the milk yield was not improved [68]. Instead, the superalimentation increased the live weight gain of the gilts during lactation. These findings illustrate that feed intake is not a limiting factor for milk yield in lactating sows and that excess feed was used for body growth. In an experiment carried out at Aarhus University, Foulum, no correlation was found between feed intake and milk yield (Danielsen, not published), which also supports the fact that feed intake is not a limiting factor for milk yield of well-nourished sows.

Table 17.3. Nutrient standards per feed unit for lactating sows[1]

Amino acids[2]		**Minerals**		**Vitamins**	
Lysine	6.0 g	Calcium	8.0 g	Vitamin A	8000 i.e.
Methionine	1.9 g	Phoshporus	2.7 g	Vitamin D_3	800 i.e.
Met+Cystine	3.6 g	Sodium	1.5 g	Vitamin E	150 mg
Threonine	3.9 g	Chloride	2.5 g	Vitamin K_3	2 mg
Tryptophan	1.2 g	Potassium	2.5 g	Thiamine (B_1)	2 mg
Isoleucine	4.2 g	Magnesium	0.4 g	Riboflavin (B_2)	5 mg
Leucine	7.0 g	Iron	80 mg	Pyridoxine (B_6)	3 mg
Histidine	2.5 g	Copper	6 mg	Niacin (B_3)	20 mg
Phenylalanine	3.6 g	Manganese	40 mg	Biotin	0.2 mg
Phe+Tyrosine	7.0 g	Zinc	100 mg	D-Pantothenic acid (B_5)	15 mg
Valine	5.0 g	Iodine	0.2 mg	Folic acid	1.5 mg
Crude protein	110 g	Selenium	0.2 mg	Vitamin B12 (B_{12})	20 µg

1) According to www.pigresearchcentre.dk
2) Amounts of amino acids and crude protein refer to ileal digestible content

Sub-optimally fed sows: Sows fed approximately 60-85% of the required level (of energy, protein, essential amino acids or other nutrients) may be regarded as sub-optimally fed. Suboptimal nutrition may be present either if the feed intake is low, if the diet is improperly balanced with nutrients, of if the body condition score is either too low or too high due to improper feeding in previous reproductive cycles. The milk yield of these sows is influenced negatively, but the impact on milk yield depends on which nutrient is the limiting factor and on the body condition of the sow (i.e. whether the sow is able to counterbalance improper feeding by increasing the mobilization of e.g. fat, protein and minerals from the body). The effect of suboptimal feeding on milk yield is hard to demonstrate experimentally due to the numerous factors that affect milk yield of sows. Specific effects of improper nutrient supply will be discussed under malnourished sows. The milk yield of sub-optimally fed sows may be enhanced via feeding with the same strategies as optimally fed sows. In addition, increased feed intake may compensate for improper dietary composition in sub-optimally fed sows if, for instance, an essential amino acid is the limiting factor. However, in sub-optimally fed sows it is more likely that less mobilization is observed with increased feed intake rather than increased milk yield because nutrient requirement for milk production is prioritized higher than conservation of body depots. It is also important to stress that suboptimal feeding for an extended period of time (e.g. throughout gestation) will decrease the body condition of the sow, which in turn will reduce the milk yield [48].

Malnourished sows: Sows severely restricted in nutrients will have a lower milk yield, no matter whether the dietary restriction is energy or protein or minerals. For instance, severe restriction of dietary lysine (from 45 to 15 g lysine/day) reduced the milk yield from 8.79 to 7.87 kg/day on day 8 of lactation and from 9.56 to 7.42 on day 18 of lactation [48]. Similarly, severe restriction of feed (i.e. severe restriction of energy, protein and other nutrients) reduced the milk yield from 8.3 to 7.0 kg/day on day 7 to 14 and from 10.1 to 6.6 on day 18 to 24 [88]. In these studies, performance of malnourished sows was compared with well-nourished sows, but that does not mean that the lysine or feed supply is normally the limiting factor for milk production in well-nourished sows. And in general, it is not recommendable to supply sows with dietary lysine (or protein) above their requirement due to economic and environmental considerations. Another study nicely illustrates how nutrition and mobilization of nutrients interact and how sows compensate for improper feed supply by increasing the nutrient mobilization from the body. Sows were fed one of six levels of feed (1.5 to 4.8 kg/day) during lactation [41]. Interestingly, the milk protein content (N x 6.38) was not negatively influenced by low feed intake and the growth rate of piglets (indirect measures of milk yield) was similar among the treatment groups during the first three weeks of lactation (Table 17.4). Only in the fourth week of lactation a depressed growth rate of piglets was observed, and only for sows ingesting less than 2.9 kg/day. The study also illustrated how well the sows were able to counterbalance the low feed supply by increasing mobilization of fat (back fat) and muscle tissues (maternal N balance).

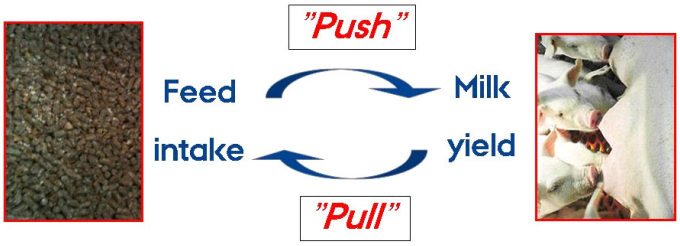
Table 17.4. Effects of sow feed intake during lactation on sow and piglet performance (data from [41]).

	Daily feed intake during lactation (kg/day)						
	1.5	**2.2**	**2.9**	**3.6**	**4.3**	**5.0**	**Significance of linear effect**
Sow live weight d1, kg	156.6	150.9	151.2	150.8	151.4	153.2	
Weight loss in lactation, kg	44.5	30.8	27.4	19.6	15.8	9.0	**
Back fat loss in lactation, mm	8.9	7.1	6.4	5.7	4.2	4.0	**
Sow nitrogen balance, g/d	-45.4	-39.0	-29.6	-27.8	-20.2	-15.5	**
Nitrogen in milk, g/kg	9.8	9.2	8.3	8.8	9.3	8.2	*
Piglet growth rate d0-21, g/d	180.9	177.1	191.9	185.2	209.7	192.9	
Piglet growth rate d21-28, g/d	136.2	155.6	184.0	193.3	193.5	192.7	*[1]

1) A quadratic effect was also significant for piglet growth rate days 21-28 ($P < 0.01$)

5.5. Milk yield and feed intake – push or pull

The good question is: how can we improve the milk yield of sows? In practice, a high yielding sow has a high milk yield, a high feed intake and a high weight loss during lactation, but it is not clear how milk yield, feed intake and weight loss interact. In mal-nourished sows, the milk yield may be improved by enhancing the feed intake, which is known as a PUSH effect (a higher feed intake increases the milk yield; Figure 17.10). In contrast, the milk yield of optimally fed sows cannot be enhanced further by increasing the feed intake. In fact, at high feed intake, the relation between feed intake and milk yield is the reverse, i.e. a high milk yield in well-nourished sows stimulates the sows' feed intake (known as a PULL effect). Therefore, the way to enhance performance of lactating sows is to stimulate their milk production! Some attention has been given to feeding strategies throughout lactation. Different feeding strategies have been tested, for instance the optimal time for introducing ad libitum feeding. Sows had a higher milk yield if ad libitum feeding was introduced one week after parturition compared to before or at parturition [16]. The mechanism is not clear, but a feeding level in late gestation that is too high seems to be associated with a higher risk of developing metritis-mastitis-agalactia complex. Also, the experiment revealed detrimental effects for the milk yield when ad libitum feeding was introduced too late, and this is likely due to depletion of body pools of fat and protein.



Figur 17.10. Relationship between feed intake and milk yield. For malnourished sows, the relation is PUSH, but in well-nourished sows the relation is PULL.

If the sows' intake of energy, protein and minerals does not meet their requirements for these nutrients, the sows will mobilize fat from adipose tissue, proteins from muscle tissues and minerals from bone tissue. Sows that mobilize nutrients from body pools of protein and fat lose weight during lactation, whereas mobilization of minerals is hardly detectable using the live weight. However, it should be emphasized that the weight loss throughout lactation ideally should be kept within a certain range (approx. 15-25 kg over 28 days), because excessive depletion of fat and protein pools will delay the return to oestrus after weaning and the performance during the subsequent reproductive cycle. On the other hand, if body mobilization becomes too low (or the sow gains live weight during lactation), the actual milk yield seems to be compromised.

Previously, mobilization of fat and protein from body pools was regarded as a negative consequence of sub-optimal feeding, but recent findings indicate that sows must mobilize nutrients from their own body to utilize their potential for milk production. Due to natural selection, it is common for all mammals to gain weight during pregnancy (mainly foetal growth, but also build-up or replenishment of maternal fat and protein pools), whereas mammals lose weight during lactation because of the massive secretion of nutrients in the milk. The sow is no exception to this pattern. Indeed, the massive amounts of energy secreted via milk are higher for sows than other mammals at peak lactation when accounting for live weight differences (Figure 17.11).

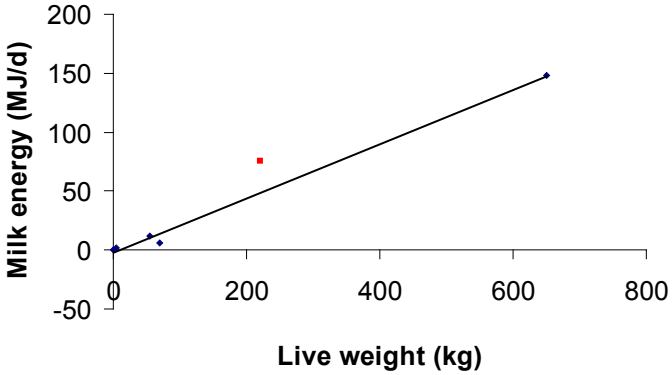


Figure 17.11. Maximum daily secretion of energy via milk in different species (rat, rabbit, goat, human, sow and cow). The figure clearly illustrates that sows (red point) produce more milk than would be expected based on their live weight when compared to various species (solid line represents the trendlines for all species except the sow).

5.6. Body condition and lactation persistency

The body condition of reproductive sows changes throughout the reproductive cycle (Chapter 2), and during gestation, sows gain weight. Early and mid-gestation is an ideal period for adjusting the feeding level for each individual sow in order to reach an appropriate condition before farrowing. At late gestation, the sows should appear well conditioned, but not fat. If the sows become too fat, they will face problems during farrowing, their feed intake throughout lactation will be too low and this may lead to reproductive problems. Conversely, if the sows are too thin at farrowing, their milk production will be reduced [42]. A likely explanation is that nutrient mobilization inadequately supports milk production during the course of lactation due to depleted body pools of fat, protein and minerals. Most sows are not as low in body condition as those in the study by Klaver and coworkers, and typically the effects of low body condition become most prominent in the fourth week of lactation, when mobilizable pools of fat, protein and minerals are exhausted. In a recent experiment, a positive correlation between sow body condition before farrowing and piglet weight gain at peak lactation was found [31]. This result emphasises that body condition is important for lactation persistency.

If sows have been fed suboptimally or are malnourished for an extended period of time, their body condition is not optimal. If the energy supply has been scarce, their fat depots are too low [42], and if they have been restricted with dietary protein or essential amino acids, their ability to support milk production by mobilising body protein is scarce [48]. If depots of body fat or body proteins become depleted, the milk production is compromised as lactation progresses, and it often leads to a reduced yield of milk in the fourth week of lactation [88], [41], [31], [32].

Body condition is surveyed in sow herds, either by visual inspection of the sows, by physically evaluating the back fat level, or by using an ultrasound scanner to assess back fat levels. Without any doubt, ultrasound scanning is the best available method currently. However, none of the methods perform very well in terms of eliminating the individual variation in body condition. Part of the explanation is related to the housing facilities in modern pig accommodation because sows nowadays are group-housed during gestation. Thus, if fed in groups, the dominant sows eat a lot more feed than their demand, whereas other sows eat much less. However, that is only a problem on some farms and many farms do have the possibility to feed the sows individually even though sows are group-housed.

6. Comparison between colostrum and milk

As described in sections 3 and 4, colostrum is synthesized prepartum, whereas milk is produced postpartum. Even though these secretions are both produced in the mammary glands and have the same major constituents (protein, lactose and fat), it is important to distinguish between production of colostrum and milk – partly because colostrum and milk play different physiological roles for the piglets and partly because nutrition and nutritional status of the sow affect colostrum and milk production differently (Table 17.5). It is important to stress that a dietary compound or intrinsic sow factor that is beneficial for the colostrum yield may be detrimental to the milk yield or vice versa.

Table 17.5. Differences in chemical composition and stimulatory factors for colostrum and milk.

	Colostrum	**Milk**
Composition		
Lactose content	Low (3%)	High (6%)
Protein content	HIgh (15%)	Low (6%)
Immunoglobulin content	High (73 mg/ml)	Low (11 mg/ml)
Dry matter content	High (23-32%)	Low (18-20%)
Yield		
Production rate	2.5-5 kg over 1 or more weeks	5-15 kg/day
Dietary MCFA[1]	↑ colostrum yield	No effect on milk yield
Dietary fibre	↑ colostrum yield	No effect on milk yield
Dietary HMB[2]	↑ colostrum yield	↓ milk yield
Sow back fat	No effect on colostrum yield	High back fat ↓ yield d 7 to 10
		High back fat ↑ yield d 10-28
Importance for piglets	Energy: Survival d 0 to 2 ↑	The main role of milk nutrients is to enhance growth, but survival is also an issue, especially during the first week of lactation
	Igs: Survival until weaning ↑	
	Growth factors: Ensures growth and development	

1 Medium chain fatty acids
2 Hydroxy methyl butyrate

7. Mammary nutrient uptake and milk synthesis

The mammary gland, as other extra-hepatic tissues, is supplied with nutrients from the blood and therefore has to share or compete with other tissues for these substrates. Milk synthesis occurs in the secretory cells of the mammary gland, which are organised in structures called alveoli around an alveolar lumen. The synthesized milk is secreted into the alveolar lumen and stored here in between sucklings. The individual milk components (lactose, protein and fat) are synthesized from nutrients supplied to the mammary gland with the blood, and the quantitative amount of nutrients taken up by the mammary gland depends on the mammary blood flow and the so-called AV-difference, where AV difference is the difference in plasma (or serum) nutrient concentration between the arterial (A) blood supplying the udder and the venous (V) blood draining the udder again. Numerous studies have been conducted with ruminants to identify the major precursors for milk synthesis and to understand how these precursors efficiently can be converted into milk components. Similar studies in the sow are very scarce, since the vascular system in the sow is much more complex with several different arteries supplying blood to each individual mammary gland and several different veins draining each gland. The major nutrients taken up by the mammary gland and the metabolic pathways are depicted in Figure 17.12, and this will be described in the following. The biochemical, stoichiometric details for many of these metabolic pathways (synthesis of protein, triacylglycerol (TAG), fatty acids de novo as well as oxidative pathways) are given in Chapter 14.

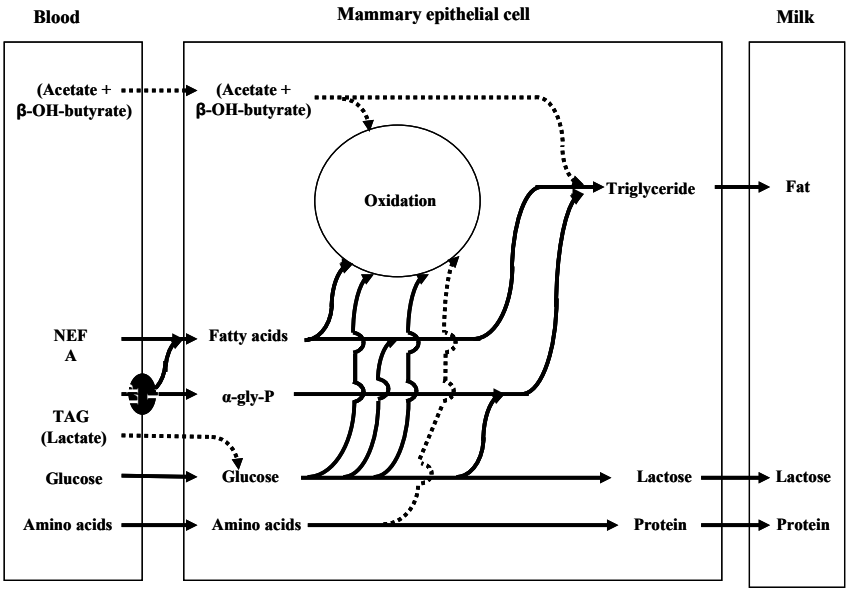


Figure 17.12. Major metabolic pathways in the mammary epithelial cell converting nutrients derived from the blood into milk components. As can be seen, lactose is synthesized from glucose, protein is synthesized from amino acids, and fat is synthesized from fatty acids 1) liberated from preformed from blood triacylglycerol (TAG) in blood lipids by the action of the capillary enzyme lipoprotein lipase (LPL) or 2) derived from non-esterified fatty acids (NEFA) in blood or 3) synthesisied de novo from glucose and 4) to an insignificant extent from the short-chain fatty acids, acetate and β-hydroxy-butyrate (β-OH-butyrate) derived from hind-gut fermentation. The glycerol backbone of milk fat is derived partly from glycerol liberated from blood TAG after activation to α-glycerol-phosphate (α-gly-P) and partly synthesized from glucose. Glucose is the dominant contributor in oxidative pathways, but fatty acids and glycerol can also contribute, whereas there is normally no net contribution from amino acids and short-chain fatty acids. Lactate can be taken up in normally small quantities, and is converted to glucose and metabolised as such.

Glucose: A high proportion (approx. 70% at 9 kg milk/day) of the total daily glucose turnover in the lactating sow is consumed by the mammary gland and this proportion can increase with milk yield (up to 80% or even more) [13]. Glucose is transported across the mammary epithelial membrane by facilitated transport by means of a glucose transporter as in other tissues. In the mammary gland GLUT1 is responsible for transporting glucose into mammary epithelial cells and GLUT1 operates independently of insulin and has a lower Km value (see Chapter 14) than the GLUT4 transporter, which is dominating in other quantitatively important tissues such as muscle and adipose (Table 17.6).

Table 17.6. Glucose transporters in peripheral tissue and their K_m-values [7].		
Transporter	K_m (mM)	Tissue
GLUT 1	1-4	Mammary tissue
		Placenta
		Red blood cells
		(Central nervous system)
GLUT 2	12-20	Pancreas
		Kidneys
GLUT 3	< 1	Central nervous system
		(Placenta)
GLUT 4[1]	4-5	Muscle tissue
		Adipose tissue

1) Insulin dependent

Consequently, the mammary gland and milk production are prioritised over other tissues in the supply and uptake of glucose, even when plasma glucose and insulin levels are high shortly after parturition [58] as discussed later. It should be pointed out that the sow, from a physiological point of view, must be considered as being in early lactation until milk production has reached its maximum 3-4 weeks after parturition (Figure 17.5). Onset of copious milk synthesis at parturition is associated with a marked upregulation of GLUT1 synthesis in the mammary gland (Table 17.7), which in turn can explain the dramatic more than 90-fold increase in de novo fatty acid synthesis from glucose over the first few days of lactation.

Table 17.7. Relationship between levels of GLUT1 mRNA expression in porcine mammary tissue in the peripartum period and level of milk production (mod. a. [13]).			
Parametre	**Day of lactation**		
	-5	2	14
GLUT1 mRNA	6.79	13.01	33.85
Milk yield (kg/day)	-	5.5	10.3
Increase in de novo fatty acid synthesis from glucose	-	93-fold (day 4)	-

Glucose is the single most important nutrient for mammary metabolism in the sow and accounts for approx. 60% of all nutrients (weight basis) taken up by the mammary gland (Table 17.8). The mammary gland extracts glucose from the arterial blood supply with reported efficiencies of 25-30% (AV-difference as a percentage of arterial plasma concentration). Mammary glucose uptake is not very sensitive towards variations in arterial glucose supply, since GLUT1 transporters can transport glucose efficiently even at concentrations below the normal physiological range, and at normal plasma glucose concentrations GLUT1 transporters will be close to saturated and operating near their maximum capacity, Vmax. Glucose uptake is therefore more closely related to the abundancy of mammary GLUT1 transporters, which in turn is related to the synthetic capacity of the mammary gland and hence development of the mammary epithelial cells during gestation and early lactation. Glucose extraction rates are therefore not constant, but will generally be expected to follow the patterns of changes in milk production during lactation as in ruminants [60], and extraction efficiencies will be inversely related to arterial glucose concentrations.

Around 53% of the glucose taken up by the mammary gland is used for synthesis of lactose [13], [71], providing both the glucose and galactose unit of this disaccharide. Lactose synthesis is catalysed by the enzyme complex lactose synthetase that consists of a catalysing unit, galactosyl transferase, and a modifying unit, α-lactalbumin, which happens to be one of the whey proteins, and lactose and milk protein synthesis are thus quite closely linked. The major part of glucose not used for lactose synthesis is oxidized (34%) [13], [51]. Glucose is the most important nutrient in the oxidative metabolism of mammary epithelial cells in sows, and in tracer studies it accounted

for 53% of total mammary CO_2 production and provided 65% of the overall energy utilised to drive milk synthesis [13], [51]. Glucose is oxidised in the citric acid (TCA) cycle resulting in generation of the majority of mammary ATP, and in the pentose phosphate pathway and malate dehydrogenase pathway (see Chapter 14) generating presumably most of the reducing equivalents, NADPH, which are required as co-factors in the de novo synthesis of fatty acids. The exact distribution of glucose oxidation between these oxidative pathways is not known. The remainder of glucose (13%) is used for de novo fatty acid synthesis and synthesis of glycerol-3-phosphate (40% derived from glucose) utilised in the final synthesis of TAG [51]. In contrast to adipose tissue, glucose is not essential as a precursor for glycerol-3-phosphate in the mammary gland, because this tissue possesses glycerol kinase activity, which means that the glycerol-3-phosphate (the remaining 60% not derived from glucose) can be formed from free glycerol originating from lipolysis of blood lipids (lipoproteins) within the gland. The fatty acids synthesized de novo are saturated with mainly 14-16 C-atoms and only insignificant amounts of fatty acids with 12 or fewer C-atoms are formed [13].

Table 17.8. Arterial blood plasma concentrations, mammary nutrient extraction and uptake for milk synthesis in lactating sows.

Nutrient[1]	Arterial plasma conc. (g/l)	AV-difference[2] (g/l)	Extraction[3] (%)	Total mammary uptake[4] (g/l milk)	Relative uptake (% of total)[5]	Reference
Glucose	1.2	0.375	31	141	61	A
Amino acids	0.37-0.66	0.151	23-41	62	24	
TAG fatty acids	0.31-0.45	0.072	16-23	27	12	
Acetate	0.013	0.006	46	2	1	
BOHB	0.018	0.002	11	-	-	
Lactate	0.12	0.014	12	5	2	
Citrate	-	0	0	-	-	
Total uptake	g/l	0-620	-	237		
	kJ[6]/l	11.23	-	4766		
Excreted in milk	kJ[7]/ll	-	-	4366		
	% of uptake	-	-	91.6		
Glucose	1.03	0.247	25	128	60	B
Amino acids	0.437	0.084	20	43	20	
TAG	0.111	0.045	41	23	11	
NEFA	0.079	0.032	40	17	8	
Lactate	0.042	0.0048	9.5	2	1	
Glycerol	0.006	0.0015	20	1	-	
Total uptake	g/l	0.414	-	214	-	
	kJ[6]/l	8.18	-	4596	-	
Excreted in milk	kJ[7]/l	-	-	4521	-	
	% of uptake	-	-	98.4	-	

1) TAG: Triacylglycerol, BOHB: β-hydroxy-butyrate, NEFA: Non-esterified fatty acids.
2) AV-difference: difference between arterial and mammary venous concentration of plasma constituents.
3) AV-difference as % of arterial plasma concentration.
4) Assuming 375 (A) or 517 (B) l plasma flow through the udder per 1 l milk secreted (equivalent to 724 l whole blood per 1 l milk secreted in B; hematocrit values = 28.6%).
5) Calculated from AV-differences.
6) Total amount of energy removed by mammary gland was estimated assuming an energy content (heat of combustion) of glucose, amino acids (α-amino acid N × 6.25), TAG, NEFA, lactate, and glycerol of 15.7, 22.4, 33.5, 39.3, 14.7, and 18 kJ/g, respectively. For TAG and NEFA, the value is for a fatty acids mixture of equal proportions of C16:0, C16:1, C18:0 and C18:1.
7) Contents in milk of lactose, fat and protein were 4.8%, 6.8% and 5.5%, respectively, in (A) and 5.7%, 5.9% and 5.3%, respectively in (B) with energy contents (heat of combustion) of 16.5, 39.3 and 23.8 kJ/g. (A) Mod. from [13] (1998; based on original data from Spincer et al. 1969: Biochem J 111:727). Milk yield unknown, but anticipated to be no more than 6 kg/day. (B) [71] (data for environmental temperature of 20 °C). Sows were 2 or 3 weeks postpartum, producing 11.1 kg milk/day with an average litter size of 12.1 piglets, had an average body weight of 4.64 kg. There were two treatments in the experiment; an ambient temperature of 20 and 28 °C. Only results for 20 °C are shown, and the sows were fed restrictedly (~ad libitum intake of sows at 28 °C).

Amino acids: The mammary gland is a dominant player in amino acid metabolism in the lactating sow. Up to 70% of the amino acids ingested with the diet are excreted in milk proteins, and for lysine the excretion in milk represents an impressive 90-95% of total lysine intake [13]. Protein synthesis in mammary tissue does not differ from protein synthesis in muscle tissue (see Chapter 14) and relies on uptake of amino acids supplied by the mammary blood supply. Amino acids are taken up by the mammary epithelial cell membrane by active transport across a concentration gradient by means of a variety of different transporters as in other tissues. It was demonstrated in one study that the mammary gland of sows expresses the CAT-1, CAT-2B, B^0,+, and ASCT1 systems during lactation, but expression levels do not seem to change from very early to peak lactation for any of these systems [65]. The efficiency of extraction varies from one amino acid to another, and is generally higher for essential amino acids (20.5%) than for non-essential amino acids (16.8%) (Table 17.9). The mammary uptakes of a number of the essential amino acids, particularly branched-chain amino acids (valine, leucine, and isoleucine), are in excess of their secretion into milk protein. Non-essential amino acids, however, are generally taken up in smaller quantities than their output in milk (Table 17.9). Hence, transamination must take place in the mammary tissue, and especially branch-chained amino acids undergo transamination as in other peripheral tissues (Chapter 14), and their carbon skeleton subsequently utilised in oxidative metabolism. It is assumed that the extent of branched-chain amino acid oxidation does not exceed 10% of the total uptake of these amino acids in the mammary gland, and it is not associated with any net-loss of α-amino-N, since it is preceded by transamination and formation of another non-essential amino acid. It is believed that the sow mammary gland can also acquire amino acids through uptake and degradation of small plasma peptides, but whether this source plays any role in the quantitative contribution to amino acid supply is not known [13].

Table 17.9. Quantitative uptake and excretion into milk of individual amino acids in the mammary gland of lactating sows.

		Renaudeau et al., 2003					Trottier et al., 1997			
	MW	**Output in milk**		**Uptake from arterial blood**			**Total output in milk**		**Uptake from arterial blood**	
		g/l milk[1]	Total output, mol/d[1]	Plasma con-centration	Extraction %	Total uptake, mol/d[2]	g/d	mol/d	g/d	mol/d
Essential amino acids (EAA)										
Lysine	169.68	3.57	0.233	36.00	21.5	0.23	23.4	0.138	23.4	0.14
Methionine	149.21	1.06	0.079	9.60	20.2	0.07	6.5	0.044	6.5	0.04
Tryptophan	204.23	0.65	0.035				8.4	0.041	8.4	0.04
Threonine	119.12	2.02	0.188	31.90	12.8	0.20	12.1	0.102	15.9	0.13
Leucine	131.17	4.19	0.355	28.60	37.1	0.44	25.7	0.196	36.5	0.28
Isoleucine	131.17	2.09	0.177	19.60	28.7	0.24	12.1	0.092	18.4	0.14
Valine	117.15	2.61	0.247	37.00	18.0	0.32	15.4	0.131	21.2	0.18
Arginine	174.21	2.87	0.183	41.60	17.2	0.22	14.7	0.084	31.2	0.18
Histidine	155.16	1.30	0.093	21.10	17.3	0.12	7.6	0.049	7.6	0.05
Phenylalanine	165.2	1.92	0.129	14.20	32.5	0.15	11.5	0.070	15.5	0.09
EAA total	-	22.3	1.72	239.60	20.5	1.99	137.4	0.947	184.6	1.28
Average MW[3]			143.8			141.7		145.1		144.5
Nonessential amino acids (NEAA)										
Alanine	89.09	1.71	0.213	-	-	-	10	0.112	22	0.25
Aspartate+asparagin	133.1	3.89	0.324	-	-	-	29	0.218	14	0.11
Cystine	175.64	0.63	0.040	-	-	-				
Glutamate+glutamine	147.13	10.18	0.768	-	-	-	63	0.428	77	0.52
Glycine	75.05	1.59	0.235	-	-	-	11	0.147	15	0.20
Proline	115.13	5.61	0.541	-	-	-	36	0.313	27	0.23
Serine	105.09	2.49	0.263	-	-	-	16	0.152	16	0.15
Tyrosine	181.2	2.07	0.127	-	-	-	13	0.072	13	0.07
NEAA total	-	28.2	2.51	263.90	16.8	2.04	178	1.442	184	1.53
Average MW[3]			124.5			124.5		123.5		120.0
Amino acids total	-	50.4	4.23			4.03	315.4	2.388	368.6	2.81
Average MW[3]			132.8			133.1		132.1		131.1

1) Calculated based on a milk protein (N x 6.38) content of 5.5% and a total daily milk production of 11.1 kg. 2) Assuming a mammary plasma flow of 517 l/l produced milk and a daily milk yield of 11.1 kg.
3) MW: Molecular weight (g/mol).

Mammary uptake of amino acids will in contrast to glucose increase linearly with increasing arterial plasma concentration, and extraction rates are therefore quite stable. The Km values for the valine and lysine transporters in sow mammary tissues are 2 and 10 times higher, respectively, than normal physiological plasma concentrations of these amino acids, and it is therefore unlikely that carrier capacity can become a limiting factor for amino acid uptake even at high dietary protein supplies. Unfortunately, protein synthesis in the mammary gland is not linearly related to arterial amino acid supply. When mammary uptake increases, amino acids will to a larger extent be oxidised in the mammary gland. Milk protein percentage is thus not very sensitive to feeding in upwards direction when amino acids are fed in excess of recommendations, whereas efficiency of transfer of absorbed amino acids into milk proteins obviously decreases when protein synthesis has reached its limit (Table 17.10). It is interesting in Table 17.10 to notice that during severe protein deprivation, 75% more lysine can be excreted in milk than supplied in the diet, and without very dramatic effects on milk yield. This must reflect a substantial capacity in the sow for redirection of non-mammary protein reserves to sustain milk protein synthesis when dietary supply of amino acids is scarce.

Table 17.10. Impact of dietary crude protein on mammary uptake of amino acids relative to their excretion into milk (data from [28]).

	Crude protein content in diet (% of DM)			
	7.8	13.0	18.2 (normal)	23.5
Dietary intake				
Feed, kg/day	4.62	5.75	4.67	4.62
Protein, kg/day	0.366	0.750	0.845	1.070
Lysine[1], g/day	18.9 (0.41)	38.5 (0.67)	42.0 (0.90)	55.0 (1.19)
Valine[1], g/day	21.3 (0.46)	40.8 (0.71)	44.8 (0.96)	55.9 (1.21)
Methionine[1], g/day	8.32 (0.18)	15.5 (0.27)	15.9 (0.34)	19.4 (0.42)
Excreted in milk				
Milk yield d11, kg/day	10.03	13.07	10.57	12.99
Milk yield d21, kg/day	9.18	13.21	10.82	12.43
Milk true protein, %	4.53	4.51	4.94	5.02
Lysine, % of dietary lysine	175	116	97.8	91.8
Valine, % of dietary valine	130	93.4	73.0	73.7
Methionine, % of dietary methionine	133	96.1	84.3	92.2

1) Dietary content of amino acid (on as-fed basis) is given in parenthesis.

Compared with muscle tissue, the rate of proteolysis in the mammary gland is much lower than the rate of synthesis, because milk proteins accumulate in secretory vesicles together with lactose. These vesicles fuse with the apical membrane of the mammary epithelial cell during excretion, and their contents are released into the alveolar lumen. In this way, milk proteins are protected against hydrolysis. It has been estimated that the rate of proteolysis in the mammary gland of sows is about one third of the total protein synthesis rate [27] similar to estimates found in ruminants [63]. Branched-chain amino acids as valine can apparently inhibit proteolysis, and thus increase the protein synthesis-to-milk protein excretion efficiency [27]. Insufficient supply of limiting amino acids, such as lysine will, on the other hand, decrease the protein synthesis-to-milk protein excretion efficiency due to reduced rate of protein synthesis [27].

Fatty acids: The last group of nutrients of quantitative importance for milk formation is the preformed long-chain fatty acids derived mainly from circulating blood lipoproteins (chylomicrons carrying absorbed fat from the gut and Very Low Density Lipoproteins transporting fat exported from the liver). Triacylglycerol (TAG) in lipoproteins are hydrolysed by the mammary capillary enzyme lipoprotein lipase, whereafter the fatty acids can be taken up by the mammary epithelial cells by passive diffusion or a facilitated carrier mechanism driven by the concentration gradient, ie. plasma

concentration. Fatty acids can also be derived from degradation of body fat and contribute to mammary fatty acid supply in the form of non-esterified fatty acids (NEFA) (Table 17.8, reference B), which circulate in plasma associated with albumin. NEFA are long-chain and relatively saturated, predominantly C16:0, C16:1, C18:0 and C18:1. NEFA is presumably only of quantitative importance in situations where plasma NEFA concentrations are sufficiently high to drive mammary uptake, and this is the case in early lactation in sows with substantial mobilization of body fat. When sows are in energy balance, NEFA concentrations will be low and AV-differences across the mammary gland close to zero. Dietary and body fat composition can be determinants of pattern of fatty acid in milk fat since they are utilised directly in TAG formation in the mammary epithelial cells. It is currently unknown if the sow mammary gland contributes to synthesis of monounsaturated fatty acids by dehydrogenation as in ruminants [11], but in general the fatty acid composition of milk reflects rather well the fatty acids supplied via the diet [50].

The contribution from glucose to de novo fatty acid synthesis is described above. In addition, acetate and β-hydroxy-butyrate derived from hindgut fermentation can be used as substrates in de novo fatty acid synthesis as in ruminants. The mammary gland actually extracts acetate very efficiently, but, despite this, the quantitative contribution to mammary nutrient uptake of acetate and β-hydroxy-butyrate is totally insignificant, as shown in Table 17.8, since diets fed to lactating sows do not normally give rise to high levels of short-chain fatty acids (from hindgut fermentation) in peripheral plasma.

The synthesis of triacylglycerol from acyl-CoA and glycerol-3-phosphate in the mammary gland is not different from the synthesis in adipose tissue (see Chapter 14). However, the rate of lipolysis is expected to be very low as in ruminants, because most of the synthesized TAG is organized in micelles that migrate to the apical membrane. These fat droplets are then surrounded by part of the cell membrane and secreted into the alveolar lumen. By this mechanism, the milk fat is protected from the action of hydrolytic enzymes, just as lactose and milk proteins. The contribution to milk TAG synthesis in the sow mammary gland from fatty acids synthesized de novo within the mammary gland relative to preformed fatty acids taken up from circulating plasma lipids is not known. Special experimental approaches would be required to address this question in sows since the fatty acids synthesized de novo have similar chain lengths as fatty acids taken up from plasma lipids. It has been speculated without much scientific evidence that de novo fatty acid synthesis can account for anywhere between 10 and 50% of total milk fatty acids, and this would be similar to the ruminant and presumably dependent on the relative supply of the different precursors. In a study focusing on utilization of dietary nutrients at the entire animal level, the de novo synthesis of fat accounted for 63% and 18% of that secreted in milk in sows fed a diet with 3 and 11% dietary fat, respectively [79]. However, in that study it was not possible to distinguish between fat de novo synthesized in liver and in the mammary glands.

Milk fat is the organic component in milk showing the greatest variation in content, and it is the most sensitive component towards variations in substrate supply. Synthesis of milk fat and relative incorporation of different fatty acids depend on the supply of the lipogenic substrates glucose, TAG and NEFA. The mammary uptake of preformed fatty acids is, as mentioned, positively correlated to arterial concentrations. Fat percentage in milk can therefore successfully be increased from the normal 6.5 to 10% or even more by addition of fat to the diet, and this will generally not have any major impact on neither protein nor lactose content in the milk [4].

Lactate has been shown to be taken up by the mammary gland. However, as can be seen in Table 17.8, the quantitative contribution has amounted only to approx. 1.5% of the total energy uptake in sows fed an energy restricted diet and even lower in sows fed according to norm, and it would indicate that lactate uptake in the mammary gland increases with output from muscle metabolism when energy supply is restricted. In one study by Linzell et al. [51], lactate uptake was almost 8 fold (0.108 g/l whole blood) higher than the highest values in Table 17.8 for unknown reasons, but in this case lactate could account for around 11% of total mammary energy uptake.

7.1. Quantitative model of nutrient metabolism in the mammary gland

Table 17.11 represents an attempt to model nutrient metabolism in a lactating sow in early lactation (week 2-3) with a daily production of 11 kg milk with 726 g (6.6%) fat; 572 g (5.2%) true protein; and 638 g (5.8%) lactose based on the current state of knowledge on mammary metabolism in sows. Details of assumptions based on text book information on biochemical pathways are given as footnotes to Table 17.11. Two different scenarios are outlined highlighting conflicting results particularly with respect to lipid metabolism and contribution of individual nutrients in the oxidative metabolism of the mammary gland (ATP production and CO_2 formation):

Scenario 1: Assuming daily mammary metabolism of glucose and amino acids, and uptake of plasma triglyceride (TAG) are as reported in previous studies

1. Glucose uptake: estimated from lactose production, using the previously reported values (see above) for mammary glucose metabolism: 53% utilised for lactose synthesis, 34% oxidised, glucose provides half of the glycerol incorporated into milk fat, and the remainder is used for de novo fatty acid synthesis.

a. Glucose uptake: 638 g lactose/[342g/mol] *2[glucose/lactose]/0.53 => 7.04 mol.This value corresponds to an uptake of 115 g/l milk, which agrees reasonably well with results obtained in experimental studies (Table 17.8).

b. Glucose oxidation: 34% of 7.03 mol glucose => 2.39 mol.

c. Glucose for glycerol synthesis: 50% of 0.86 mol glycerol (see 4b below for calculation), 2 glycerol per glucose => 0.21 mol glucose used.

d. Glucose used for de novo fatty acid synthesis: (7.04 [total uptake] -3.73 [lactose] -2.39 [oxidation] -0.21 [glycerol]) mol => 0.70 mol.

2. Amino acid uptake: calculated from milk protein synthesis in the two scenarios assuming a 1:1 ratio between net α-amino -N uptake and net α-amino -N excretion in milk protein, ie. no net oxidation of amino acids, and an average MW (see Table 17.7) of 132 and (132-18) g/mol for free and protein-bound amino acids, respectively (correction for exclusion of 1 mol of H_2O during peptide bond formation).

a. Amino acid uptake: 572 g true protein/[132-18] g/mol => 5.02 mol. This corresponds to an uptake of 60 g/l milk, which is very similar to values obtained in several experimental studies (Tables 17.8 and 17.9).

3. De novo fatty acid synthesis: calculated from 0.70 mol glucose (see 1d), while contribution of short chain fatty acids (acetate and β-hydroxy-butyrate) is negligible (Table 17.8) and ignored.

a. 2 mol acetyl-CoA precursors (C2) are generated per mol glucose => 4 C-atoms.

b. Fatty acids synthesized: average chain length of 17 C-atoms ie. 0.70 mol glucose x (4 C-atoms from glucose/17 C-atoms on average per fatty acid synthesized) => 0.17 mol. This represents a contribution of 6.42% de novo out of total milk fatty acids. As mentioned above, values of 18 and 63% for sows fed diets with high and low fat content, respectively, agree quite well with up to 50% as proposed by Boyd and Kensinger [13]. The estimated contribution of glucose to de novo fatty acid synthesis in this scenario is therefore hardly realistic, and would require a far higher glucose uptake and/or much lower proportion of glucose utilised for oxidation.

Table 17.11. Quantitative model of nutrient uptake in the mammary gland and use of individual nutrients for synthesis of milk components, ATP production and contribution to CO_2 production for a sow producing 11 kg milk (5.8% lactose, 5.2% protein and 6.6% fat). Estimations are given for two scenarios using different assumptions (highlighted in blue). Values critical for evaluation of the validity of the two scenarios modelled are highlighted in red.

Daily milk yield	**11**	**kg/d**	**Milk components excreted in milk (mol/d) and total energy output in milk (Mj/d):**																				
Lactose % & MW*	5.8	342	Lactose	1.87	Amino acids	5.02	Fatty acids (FA)	2.57	Glycerol	0.86	Total milk energy***	52.7											
Protein % & MW*	5.2	114	Nutrient and ATP consumption** for synthesis of milk constituents (mol/d):											Nutrient oxidation and ATP production (mol/d)							Contribution to CO_2 production		
Fat % & MW*	6.6	848	Lactose		Protein		Lipid						Total ATP consumption	Glucose		Fatty acids		Glycerol		Total ATP production**	Glucose mol/d	FA mol/d	Glycerol mol/d
Weight loss: approx. 1 kg/d (mostly fat)							De novo FA		Preformed FA		Glycerol				ATP		ATP		ATP				
Nutrient uptake	mol/d	g/l milk		ATP		ATP		ATP		ATP		ATP											
Scenario 1: Glucose uptake is used for lactose synthesis (53%), oxidation (34%), supplies 50% of milk fat glycerol and the rest is used for de novo fatty acid synthesis; TAG uptake = 27 g/l milk; NEFA supplies remaining milk fatty acids.																							
Glucose	7.04	115.2	3.73	5.60			0.70	-0.39			0.21	1.28	6.49	2.39	86.2					86.16	15.8		
Amino acids	5.02	60.2			5.02	40.1							40.1							0.00			
TAG	0.35	27.0							1.05	2.10	0.43	0.43	2.53			0.00	0.00	-0.08	-1.32	-1.32		0.00	-0.23
NEFA	1.35	33.2							1.35	2.71			2.71			0.00	0.00					0.00	
Total FA in milk:		2.57					6.42	% de novo of total milk fatty acids					51.9		102		0.00		-1.56	84.8	101.5 % of total	0.00	-1.50 % of total
Total energy uptake***	58.8	Mj	of which 89.6% is excreted in milk																				
Scenario 2: Glucose uptake is used for lactose synthesis (70%), de novo fatty acid synthesis (5%), supplies 50% of milk fat glycerol and the rest is oxidised; NEFA uptake ~ 17 g/l milk; 5% of NEFA and TAG derived fatty acids are oxidized.																							
Glucose	5.33	115.2	3.73	5.60			0.27	-0.15			0.21	1.28	6.49	1.12	40.3					40.3	7.24		
Amino acids	5.02	60.2			5.02	40.1							40.1							0.00			
TAG	0.65	50.0							1.85	3.70	0.43	0.43				0.10	12.8	0.22	3.74	16.5		1.65	0.66
NEFA	0.69	17.0							0.66	1.32						0.03	4.55			4.55		0.59	
Total FA:	2.64	2.57					2.44	% de novo of total milk fatty acids					49.6	% of total	65.6		28.3		6.10	61.4	71.4% of total	22.1 % of total	6.51 % of total
Total energy uptake***	56.8	Mj	of which 92.8% is excreted in milk																				

Click here to download an interactive excel sheet.

* MW: Molecular weight in g/mol
** This number includes glucose oxidised in the pentose phopsphate pathway for NADPH generation, and therefore ATP production is slightly overestimated (see taxt for further discussion.
***Calculated using the following energetic values (kJ/g; see also footnotes for Table 17.8):
Milk components: Lactose 16.5, Protein 23.8, Fat 39.3
Plasma metabolites: Glucose 15.6, Amino acids 22.4, Triglyceride (TAG) 39.3, Non-esterified fatty acids (NEFA) 39.5
(for fats derived from [24], for an even mixture of C16:0, C16:1, C18:0 and C18:1 in NEFA and milk TAG)
Biochemical assumptions underlying the calculations (for details: see text):
Synthesis of milk components:
Lactose: Synthesized from 2 glucose at a cost of 3 ATP/lactose. Molecular weight (MW: 342 g/mol)
Protein: Synthesized from free amino acids (MW: 132 g/mol) transferred in a 1:1 ratio from blood to milk and at a cost of 5 ATP/peptide bond formed.
Proteolysis quantitatively constitutes 1/3 of protein synthesis [27], ie. mammary protein synthesis is 50% higher than protein excretion in milk.
Protelolysis is associated with an expense of 1 ATP/peptide bond broken.
Fat: Preformed, long-chain fatty acids are taken up from hydrolysed plasma triacylglycerol (TAG; MW: 848 with average fatty acid chain length of C17) and from non-estierified fatty acids (NEFA).
Fatty acids are synthesized de novo from glucose providing 2 acetyl-CoA (ie. 4 C-atoms) and the remaining 2 C-atoms are released as CO_2
Preformed and de novo synthesized fatty acids have an average chain length of 17 C-atoms (divided between C16 and C18; MW: 270 g/mol).
Milk fat synthesis (esterification) costs 2 ATP per blood-derived fatty acid for activation to acyl-CoA and 1 ATP per blood derived glycerol for activation to α-glycerol-P. For de novo synthesized fatty acids and α-glycerol-P these costs are included in their costs of synthesis.
De novo fatty acid synthesis: for every glucose (see equations in Chapter 14 for details), 2 acetyl-CoA can be generated in the mitochondrion and transferred to the cytosol at a net expense of 2 ATP and generation of 2 NADH and 2 NADPH. It costs 1 ATP to activate acetyl-CoA to malonyl-CoA, ie. a total of 2 ATP for every chain elongation with a 2 C-unit, except for chain elongation from C16 to C18 (by a different route) which costs only 1 ATP, amounting to an average of 15.5 ATP for synthesis of fatty acids with an average chain length of 17 C-atoms. 8.5 NADH are also formed, giving rise to 25.5.ATP, resulting in a net production of 2.36 ATP and 2 NADPH per glucose utilised.
Synthesis of α-glycerol-P is associated with a net consumption of 6 ATP pr glucose, derived from activation of glucose (2 ATP) and the regeneration for each of the two α-glycerol-P units of 1 NAD+ (loss of 2 ATP; 1 ATP less than if NADH was formed in mitochondria due to cost of translocation from cytosol across the mitochondrial membrane).
Oxidation of nutrients and contribution to ATP and CO_2 production:
Glucose: Complete oxidation of glucose in glycolysis, citric acid cycle incl. regeneration of oxidative equivalents in electron transport chain yields 36 ATP and 6 CO_2 per glucose. MW:180 g/mol.
Glucose used for de novo fatty acid synthesis (decarboxylation of pyruvate to acetyl-CoA) releases 2 CO_2 per glucose utilised.
Glycerol: Complete oxidation yields 17 ATP and 3 CO_2 per glycerol. MW: 92 g/mol
Amino acids: There is no net oxidation of amino acids in the mammary gland. MW of free amino acids: 132 g/mol, for peptide bound amino acids: 114 g/mol (exclusion of 1 molecule of water)
Fatty acids: Oxidation of long-chain fatty acids in the mammary gland accounts for <10% of mammary uptake from blood triglycerides and NEFA.
Long-chained fatty acids (C16 and C18) taken up by the mammary gland are oxidized by β-oxidation to acetyl-CoA and further to CO_2 in the citric acid cycle releasing an average of 17 CO_2 per fatty acid.
Fatty acid oxidation (see Chapter 14 for equations) yields [8.5 x (no. of carbon atoms in fatty acid chain - 2) + 10] – [2 x no. of double bonds in fatty acid chain], which gives an average of 131.5 ATP for a fatty acid mixture with an average chain length of C17 and equal proportions of saturated and monounsaturated fatty acids.

4. Milk fat synthesis: estimation assumes that fatty acids (de novo synthesized and derived from blood lipids) have an average chain-length of 17 C-atoms in agreement with the normal fatty acid profile in sow milk, thus giving a MW of 848 g/mol milk fat (3 x 270 [fatty acids] +92 [glycerol] -3 x 18 [water released during esterification] = 848 g/mol).

a. Fatty acids in milk fat: 726 g fat/[848 g/mol] x 3 [mol fatty acid/TAG] = 2.57 mol C17.

b. Glycerol in milk fat: 1 glycerol backbone for every 3 of 2.57 mol fatty acids => 0.86 mol.

c. Mammary TAG uptake: in the range 23-27 g/L milk have been reported in high-yielding sows (Table 16.8). Using the higher value for a sow presumed to receive supplementary dietary fat => 297 g TAG ~ 0.35 mol TAG with 0.35 mol glycerol and 1.05 mol fatty acids, which are all incorporated into milk fat.

d. Glycerol: 50% derived from glucose => 0.43 mol α-glycerol-P from glucose ~ 0.21 mol glucose utilised (2 α-glycerol-P for every mol glucose utilised), The model thus accounts for only 0.78 out of the 0.86 mol glycerol excreted in milk TAG.

e. NEFA contribution to milk fatty acids: estimated as total milk fatty acids (2.57 mol) minus fatty acids derived from either plasma TAG (1.05 mol) or synthesized de novo from glucose (0.17 mol) => 1.35 mol. This is equivalent to 33.2g NEFA/L milk, which is 2-fold higher than observed in experimental studies and probably not realistic except perhaps in sows with a very high mobilization of fat and high plasma NEFA.

5. Energy consumption for milk synthesis:

a. Lactose synthesis: requires 3 mol ATP per mol lactose [47] => 3 x 638 g lactose/[342 g/mol] = 5.60 mol ATP.

b. Protein synthesis: energy requirement is calculated based on the assumption that the rate of protein synthesis in the mammary gland is equivalent to 1.5 times the rate of milk protein secretion [27] similar to ruminants [63], [8]. Thus 5.02 x 1.5 = 7.53 mol peptide bonds are synthesized concurrently with hydrolysis of 7.53 – 5.02 = 2.51 mol peptide bonds daily. ATP requirements for protein synthesis and proteolysis are 5 and 1 mol per peptide bond, respectively [52], [29] => 5 x 7.53 + 1 x 2.51 = 40.1 mol ATP for total protein turnover.

c. Milk fat synthesis from plasma derived lipids: 2 ATP are used for activation of preformed long-chain fatty acids taken up from plasma lipids (TAG or NEFA) to acyl-CoA, and 1 ATP is required to activate plasma lipid derived free glycerol to α-glycerol-P (1 mol ATP/mol glycerol) => 2 x 1.05 (TAG-fatty acids) + 1 x 0.35 (TAG-glycerol) + 2 x 1.35 (NEFA) => 2.53 + 2.71 = 5.24 mol ATP.

d. De novo fatty acid synthesis: occurs in the cytosol from acetyl-CoA, and from equations in Chapter 14 it can be derived that it is associated with a net cost of 2 ATP per glucose resulting in delivery of 2 acetyl-CoA in the cytosol, and this is also associated with formation of 2 NADH and 2 NADPH per glucose. It costs 1 ATP to activate acetyl-CoA to malonyl-CoA needed for chain elongation (2 C-atom per elongation cycle) for fatty acids up to C16 (50% of fatty acids), whereas chain elongation from C16 to C18 (50% of fatty acids) occurs by a different route and has a cost of only 0.5 ATP per C2 unit. This amounts to an average cost of 15.5 ATP for synthesis of fatty acids with an average chain length of 17 C-atoms, but 8.5 NADH are also produced giving rise to 3 x 8.5 = 25.5 ATP => net production of 2.36 ATP per glucose utilised => -2.36 x 0.17 (see 3b) = -0.39 mol ATP. Two reducing equivalents in the form of NADPH are also required for each chain elongation (addition of a 2 C-unit from acetyl-CoA derived from glucose), equivalent to 2 x (17-2)/2 = 15 NADPH for fatty acids with an average chain length of 17 C-atoms => 15 x 0.17 = 2.48 mol NADPH.

This NADPH is synthesized from glucose in the pentose-phosphate pathway or in the isocitrate cycle across the mitochondria. The relative contribution from these two pathways in the sow is not known. The NADPH balance is not specifically included in Table 17.11, and calculated ATP production from glucose is therefore slightly overestimated. Generation (from glucose) of the precursor acetyl-CoA in the cytosol also generates 1 NADPH for every acetyl-CoA formed, and half of the NADPH is thus provided for associated with formation of acetyl-CoA. Oxidation of 1 mol glucose in the pentose-phosphate pathway can yield 3 mol CO_2 + 1 mol glyceraldehyde-3-P + 6 mol NADPH => (0.5 * 2.48)/6 = 0.21 mol glucose would be needed for synthesis of the required NADPH. ATP production from glucose is reduced with 18 (representing ATP production potential from the one half of glucose released as CO_2) plus 1 (representing the amount of ATP generated, which could have been generated during metabolism of half a glucose molecule to glyceraldehyd-3-phosphate) during this metabolism of glucose in the pentose-phosphate pathway compared to the glycolytic pathway => total ATP production from glucose is overestimated with 19 x 0.21= 3.99 mol ATP.

e. Synthesis of α-glycerol-P from glucose is associated with ATP consumption for initial activation of glucose (2 ATP) and loss of ATP synthesis associated with conversion of 1 NADH formed in the cytosol to 1 NAD+ (2 ATP; NADH formed in the cytosol yields one less ATP than when formed in the mitochondrion due to a cost of 1 ATP for translocation across the mitochondrial membrane) per α-glycerol-P unit synthesized => 6 ATP consumed per glucose used => 1.28 mol ATP.

6. Pattern of nutrient oxidation and quantitative mammary energy metabolism:

a. Glucose oxidation (36 ATP and 6 CO2 per glucose): was pre-set at 34% (2.39 mol) of total uptake according to previous studies => 36 x 2.39 = 86.2 mol ATP. Total mammary CO_2 production (15.8 mol) was likewise derived entirely from glucose oxidation, with 14.4 mol from complete oxidation of 2.39 mol glucose and 1.40 in association with de novo fatty acid synthesis, where 2 CO_2 are released when 2 pyruvate are decarboxylated to 2 acetyl-CoA. This is in line with classical tracer studies from the 60es [51] with reported RQ values for the sow mammary gland close to 1. However, according to the same tracer studies, glucose oxidation could only account for 54% of total mammary CO_2 production, demonstrating that although it is the most important substrate, there must be other nutrients metabolised in oxidative pathways in the sow mammary gland. Labelled C can in tracer studies be exchanged with non-labelled C from other precursors in certain steps of metabolic pathways, and the contribution of glucose to CO_2 production thus underestimated, but it is also likely that other substrates as fatty acids, lactate, branch-chained and deaminated glucogenic amino acids (on high protein diets) can contribute to mammary energy metabolism. Modern sows with a substantial higher milk production than in the old studies as well as a presumably higher mobilization (1-2.4 kg/d in studies reported in Tables 17.7 and 17.8) could very well give rise to substantially higher uptakes of preformed fatty acids from plasma lipids, suppressing the entry of glucose into oxidative pathways as well as its use for de novo fatty acid synthesis. In the present model, the contribution of lactate has been ignored due to the insignificant contribution to nutrient uptake reported previously (2%; see Table 17.8). But in one study by Linzell et al. [51], lactate did contribute with as much as 11% of mammary energy uptake.

b. Total ATP consumption was substantially lower (51.9 mol) and amounted to only 61.2% of total ATP production (84.8 mol). This suggests that the assumption that glucose consumption is distributed with a constant rate of 53% for lactose synthesis and 34% for oxidation may not be correct. It is plausible that the relative proportion utilised for lactose synthesis may be higher in modern sows with a higher milk production and a high mobilization of body fat in early lactation due to suppression of glucose consumption for de novo fatty acid synthesis as well as inhibition (mass-action) of glucose entry into oxidative pathways.

c. Mammary energy efficiency (total milk energy output [52.7 MJ] divided by total energy content in nutrients taken up by the mammary gland [58.8 MJ]) amounted to 89.6%, using the energetic contents (heat combustion) for nutrients and milk components. This is in fairly good agreement with efficiencies reported in other studies of mammary nutrient conversion into milk.

Scenario 2: Assuming mammary glucose metabolism is distributed with 70% for lactose synthesis, 5% for de novo fatty acid synthesis, and contributing to synthesis of 50% of milk fat glycerol, and additionally assuming that 5% of total preformed fatty acids taken up are oxidized in the mammary gland and NEFA uptake amounts to the 17 g/L milk reported in previous studies:

1. Amino acid uptake, contribution of glucose and TAG-derived glycerol to milk fat glycerol, ATP consumption for milk component synthesis, and ATP and CO_2 production from glucose are estimated as in scenario 1.

2. Glucose uptake and metabolism: calculated as in scenario 1, but assuming now that 70% of glucose is used for lactose synthesis => 5.33 mol glucose uptake, of which 3.77 ~70% are used for lactose (as in scenario 1), 5% ~ 0.27 mol for de novo fatty acid synthesis (0.063 mol fatty acids synthesized), 0.21 mol for α-glycerol-P syntheses (as in scenario 1) and the remaining 1.12 mol are oxidised providing 65.6% of total mammary ATP production and 71.4% of mammary CO_2 production, which is closer to values previously reported (see scenario 1 – 6a) than the 100% obtained in scenario 1.

3. Total preformed fatty acid uptake: The mammary gland has a low preference for oxidation of long-chain fatty acids (<10%) in sows as also observed in ruminants. It is assumed in scenario 2 that 5% of preformed long-chain fatty acids are oxidised, since preformed fatty acids are expected to contribute to mammary oxidative metabolism particularly when mammary uptake is relatively high, driven by high blood concentrations of NEFA (as expected in the modelled sow with substantial mobilization of body fat) and TAG (as a result of relatively high intake of dietary fat) => total fatty acid uptake of (2.57-0.063 de novo)/0.95 = 2.64 mol.

4. NEFA uptake and metabolism: NEFA has been claimed to contribute little to milk fat synthesis, but a sow producing 11 kg milk will most likely be in negative energy balance with NEFA concentrations high enough to result in positive AV-differences across the mammary gland. A moderate NEFA uptake of 17 g/l milk, as reported in Table 17.4, seems realistic => uptake of 0.69 mol fatty acids, of which 95% (0.66 mol) are incorporated into milk fat and 5% (0.03 mol) are oxidised.

5. TAG derived fatty acids uptake accounts for total mammary uptake of preformed fatty acid uptake (2.64 mol) not covered by NEFA (0.69) => 1.94 mol fatty acids. Of the fatty acids taken up, 5% (0.10 mol) are oxidised, and 95% (1.85 mol) are incorporated into milk fat. TAG derived fatty acid uptake corresponds to an uptake of 50.0 g/l milk, which is not very different from the higher values reported in previous studies (Table 17.9), and it may thus be a realistic estimate.

6. Glycerol is taken up from plasma TAG (0.65 mol) of which 0.43 mol are used for milk fat synthesis (accounting for 50% of milk fat glycerol as in scenario 1) and the remainder 0.22 mol are oxidised (17 ATP and 3 CO_2 per mol) => 3.74 mol ATP (6.10% of total ATP production) and 0.66 mol CO_2 (6.51% of total CO_2 production).

7. Preformed fatty acid oxidation: ATP production from β-oxidation to acetyl-CoA units and further oxidation of acetyl-CoA units to CO_2 in the citric acid cycle yields (see Chapter 14 for equations) = [8.5 x (no. of carbon atoms in fatty acid chain - 2) + 10] – [2 x no. of double bonds in fatty acid] = average of 131.5 ATP per fatty acid for a fatty acid mixture with an average chain length of C17 and equal proportions of saturated and monounsaturated fatty acids => 131.5 x (0.10 [TAG derived fatty acids] + 0.03 [NEFA]) = 17.3 mol ATP and 2.24 mol CO_2, representing 28.3% of the total mammary ATP production and 22.1% of the total mammary CO_2 production.

8. Pattern of nutrient oxidation: appears more balanced in this scenario with glucose oxidation accounting for 71.4% of CO_2 production (assuming complete oxidation and liberation of all C-atoms as CO_2). This should be compared to estimates of 54% in older studies in sows with lower milk production. Around 65.6% of ATP generation (ignoring that a minor portion of glucose and fatty acids

is oxidized through pathways generating NADPH for de novo fatty acid synthesis) is derived from glucose oxidation.

9. Mammary efficiency: excretion of energy in milk (52.7 MJ) from energy in nutrients taken up (56.8 MJ) was estimated to be 92.8% (compared to the 89.6% in scenario 1), which also appears plausible and with an overall balance of nutrient metabolism that is much more realistic than in scenario 1.

Overall, it can be concluded that it is difficult to produce a precise quantitative model on nutrient metabolism in the lactating sow mammary gland due to lack of detailed information about particularly lipid metabolism in the mammary gland and the sensitivity of mammary uptake relative to substrate supply and sow metabolic status.

The two scenarios support that glucose must be the principal nutrient for energy metabolism (ATP and NADPH generation) in the sow mammary gland, and previous reports on contribution of glucose to CO_2 production have most likely underestimated this contribution. The two scenarios tend to suggest that de novo fatty acid synthesis within the mammary gland from glucose may be of a quite small magnitude in sows in negative energy balance and with a relatively high dietary fat intake (8% fat in DM) driving a significant mammary uptake of preformed fatty acids and their incorporation into milk fat. This however seems to conflict with the previously mentioned Danish studies, where de novo fatty acids could contribute 18-63% of fatty acids excreted in sows fed diets high or low in dietary fat [79], but as also pointed out, it was not possible in that study to determine to what extent the de novo synthesis occurred in the mammary gland or elsewhere.

7.2. Changes in priority of nutrients in sows during gestation, transition and lactation

In general, the highest priority for mammals is to maximize the number of viable offspring, and since birth weight of piglets is positively related to piglet survival, foetal growth has highest priority for sows during gestation (Figure 17.7). For a sow (a litter-bearing species), this also implies that during transition from gestation to lactation, traits that favour survival of perinatal piglets have the highest priority – i.e. 1) mammary growth (a prerequisite for mammary secretions); 2) colostrum synthesis (transfer of energy and antibodies via colostrum); and 3) provision of nutrients in milk required for growth and development of the neonate.

During the onset and course of lactation the sow undergoes extensive metabolic changes, which in early lactation favour nutrient supply to the mammary gland for milk synthesis at the expense of other body tissues. Over the course of lactation, there is a gradual shift with increasing priority on non-mammary tissues when and after milk production has peaked, which occurs around lactation weeks 3-4. During established lactation, glucose and amino acid consumption in the mammary gland can, as previously mentioned, account for approx. 70-80% of the total daily amount of glucose and amino acids ingested. To satisfy this enormous mammary demand for nutrients, the sow will generally increase her feed intake by a factor 2 or more over the first week of lactation, but despite this increase in feed intake it is normal for the modern sow (nursing 12-14 piglets and producing around 12-14 kg milk/day at peak lactation) to experience a weight loss of 0.5 to 1 kg/d on average over a 4 week lactation period. A study by McNamara and Pettigrew [56] (Table 17.12) showed that in the early lactating sow (parity 2 or higher), weight loss can primarily be ascribed to mobilization of lean tissue, and the extent of protein mobilization will increase with protein deficiency, but is apparently not very sensitive to changes in fat supply. When evaluating the data in Table 17.12, it must be recalled that protein content in lean tissues is approx. 20% and loss of lean body mass will therefore be approx. 5 times higher than protein loss (the ratio of lean-body weight loss to protein loss was approx. twice as high than this on the Norm protein diet for unknown reasons). The loss of body fat does appear to increase also on diets deficient in protein and to diminish in diets by inclusion of fat, although the differences in the study underlying Table 17.12 were not significant.

Table 17.12. Impact of dietary protein and fat on mobilization of body fat and protein in lactating sows (parity 2 and higher) (data from [56]).

Diet composition (in feed as-fed)	**Low fat (2% added) (~12.5 MJ ME/kg feed)**		**High fat (7% added) (~13.8 MJ ME/kg feed)**		**Significant effect of dietary:**
	Low protein (11.6% CP)	Norm protein (13.1% CP)	Low protein (11.6% CP)	Norm protein (13.1% CP)	
Feed intake (kg/day), wks 1->3	5.2->6.2	5.3->5.8	5.2->5.6	5.2->6.3	Fat
Sow body weight, kg					
Day 1	211	216	215	219	
Day 7	205	213	216	219	Protein
Day 14	199	206	211	215	Protein+fat
Day 20	188	197	200	207	Protein+fat
Live weight change, kg	-23	-19	-15	-12	
(loss relative to d1, %)	(10.9)	(8.8)	(7.0)	(5.5)	
Change in fat mass in total carcass, kg*	-5.0	-2.8	-0.6	+3.5	
Change in protein mass in lean, kg*	-3.0	-0.9	-3.7	-1.0	Protein
Milk production, kg/day**	9.26	10.1	9.58	10.4	
Litter weight (d1-21)	48.7	52.6	48.8	52.6	(Protein)

*)Relative to sows slaughtered day 1-3 of lactation. Changes in fat content were not significantly affected by dietary level of protein or fat. **) Calculated from litter growth as 7 + (2.50 × ADG) + (80.2 × piglet BW) [62], ie. estimated average over 21 days of lactation.

The mammary gland can thus be considered a gigantic parasite capable of extracting and metabolising nutrients even when the availability to other body tissues is low. The reason for this is that the mammary gland does not submit to the same endocrine regulation as other tissues, e.g. being independent of insulin for its uptake of glucose and amino acids.

Despite extensive loss of body weight during lactation, the sow seldom experiences problems with metabolic diseases common in ruminant animals during the first week of lactation, like ketosis and hepatic lipidosis (fatty liver). The explanation for this species difference has been ascribed to different mechanisms of so-called homeorhetic adaptation of metabolism to lactation in sows compared to ruminants. When evaluating such species differences, it must, however, be born in mind that a sow nursing her piglets undoubtedly has a more modest rate of increase in milk production from around 5.5 kg milk/day at day 2 (2.8% of body weight for a 200 kg sow) determined by the limited digestive capacity of the neonatal piglets and rising to 10.3 kg (5.2% of body weight) at day 14 of lactation determined by the synthetic capacity of the mammary glands (see Table 17.7). For comparison, it was found in a Danish study [39], [12] that milk yield in Holstein-Friesian dairy cows increased from approx29 kg/day few days after calving (4.8% of body eight for a 600 kg cow) to appr.ox6 kg on day 14 after calving (6% of body weight), and the most rapid change in body weight loss was experienced in the immediate postpartum period and could amount to >7% of body weight during the first week of lactation.

During the first week of lactation it is recommended to increase energy supply to sows from 2.5 to 5.5 FUsow and this corresponds to an availability of feed energy of approx1 feed unit for sows (FUsow) milk produced at this time point. At the peak of lactation in dairy cows the same value is around 27.3 feed units for cattle (FUc)/46.0 kg milk = 0.59 FUc/kg milk [12]. The two feed evaluation systems are not identical, but both are net energy systems and 1 FU in both systems corresponds to approx. 7.5-7.9 MJ/FU. It is therefore likely that the initiation and first week of lactation is less metabolically stressful for a sow than for a dairy cow, and that the metabolic load gradually increases to reach a maximum around weeks 3-4 of lactation for sows, when milk production and body weight loss peak, whereas the metabolic stress in a dairy cow decreases over the first 3-4 weeks of lactation, and at this time body weight reaches a nadir and energy balance gradually becomes positive for the cow.

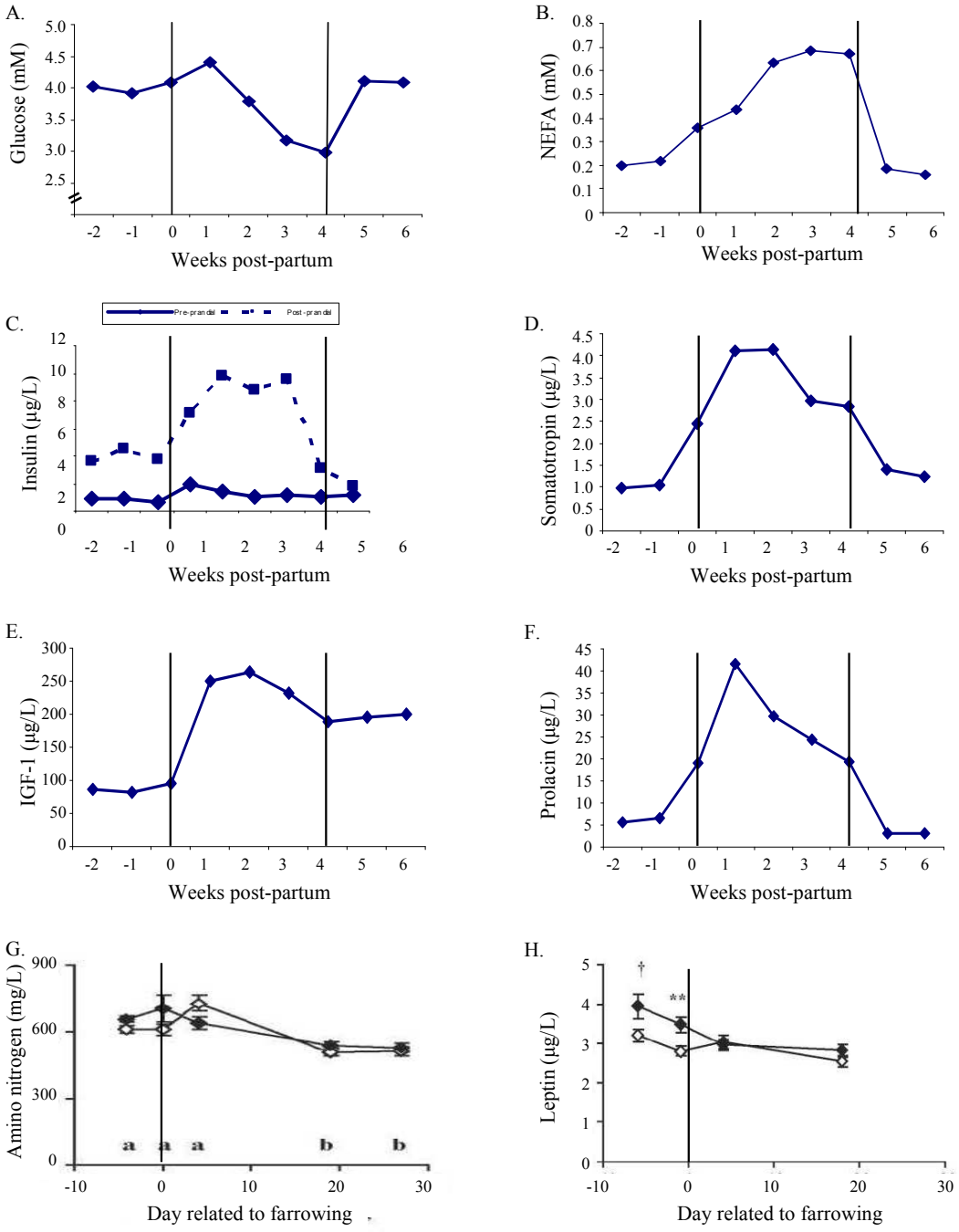


Figure 17.13. Changes in plasma concentrations of nutrients and hormones in the sow during the transition from gestation to lactation and after weaning after 4 weeks of lactation (indicated by vertical lines). A-F: modified from data from [44]. G-H: from [70].

There are distinct differences compared to observations in ruminants, which reflects the characteristics of metabolic stress imposed on the sow, and thus the differences in homeorhetic adaptations in the suckled sow compared to the dairy ruminant over the course of lactation. Figure 17.13 shows blood concentrations of important metabolites and metabolic hormones at different time points during gestation, lactation and after weaning [44]. In order to interpret these findings, a brief general introduction to the endocrine system will be given.

8. The endocrine system

Hormones are secreted from endocrine organs and transported with the bloodstream to target tissues where they bind to specific receptors and in this way affect various cellular processes. The hormonal effect depends on the number of receptors in the target tissues and the hormone supply. The mechanisms of action for steroid and thyroid hormones are similar. At their target tissue, these hormones can pass the cell membrane and bind to intracellular receptors. The hormone-receptor complex subsequently binds to nuclear DNA, which stimulates the transcription of specific m-RNA and in specific enzymes thereby affecting metabolic events within the cell. Protein hormones cannot penetrate the cell membrane, and they react with specific receptors at the surface of the cell membrane and affect the intracellular metabolism via second messengers. Table 17.13 provides an overview of major metabolic effects of some important metabolic hormones in target tissues.

Table 17.13. Effects of important homeorhetic hormones in hepatic, adipose, muscle and mammary tissues.

Hormone	Tissue	Effect[1]	Process	Mode of action[2]
Insulin	Hepatic	↓	Gluconeogenesis	Inhibition of glu-6-p
		↑	Glycogenesis	Activation of glycogen synthetase
		↓	Glycogenolysis	Inactivation of glycogen phosphorylase
		↑	IGF-synthesis	Indirectly via stimulation of synthesis of somatotropin receptors
	Adipose	↓	Lipolysis	Inhibition of hormone sensitive lipase
		↑	Triacylglycerol synthesis	Increased lipoprotein lipase activity
		↑	Glucose uptake	Stimulation of GLUT4
	Muscle	↓	Proteolysis	Decreased synthesis of protease mRNA
		↑	Protein synthesis	Increased amino acid uptake
		↑	Glucose uptake	Stimulation of GLUT4
	Mammary	-	Glucose uptake	GLUT 1 (independent of insulin)
		(↑)	Protein synthesis	Possible cross-reaction with IGF-1 receptors
Glucagon	Hepatic	↑	Gluconeogenesis	Activation of glu-6-p and stimulation of amino acid oxidative deanimation
		↓	Glycogenesis	Inactivation of glycogen synthetase
		↑	Glycogenolysis	Activation of glycogen phosphorylase
	Adipose	-?	Lipolysis?	Presumably no significant effect
Somatotropin	Hepatic	↑	IGF-1 synthesis	
		↑	IGF-binding protein 3	
	Adipose	↑	Lipolysis	Increased effect of catecholamines
		↓	Triacylglycerol synthesis	Decreased activity of lipoprotein lipase
	Muscle	↓	Glucose uptake	Decreased sensitivity of insulin
		↑	Proteolysis	
		↑	Protein synthesis	Mediated via IGF-1?
	Mammary	-		No receptors
IGF-1	All tissues (?)	↑	Growth	Stimulates cell proliferation Inhibits programmed cell death
	Adipose	-		No receptors
	Muscle	↑	Protein synthesis	mRNA synthesis
		↓	Proteolysis	
	Mammary	↑	Milk synthesis	Increased blood flow to the organ Generally increased metabolic activity
T_3 & T_4	Adipose	↑	Lipolysis	
		-	Lipogenesis	
	Muscle	↑	Proteolysis	mRNA synthesis and ATP generation
		↑	Protein synthesis	mRNA synthesis and ATP generation
	Mammary	?		Receptors?

1) () stimulation, (¯) inhibition or (-) no effect on the process in question. 2) Glu-6-p: Glucose-6-phosphatase.

8.1. Insulin

Insulin is an anabolic hormone, favouring uptake of glucose, amino acids and fatty acids in non-mammary tissues, and stimulating deposition of glycogen, protein and lipids in its target tissues (see Table 17.13). Insulin (Figure 17.13C) is the key regulatory factor (in concerted action with glucagon) in defence of glucose homeostasis. When plasma glucose concentration is high, secretion of insulin from the β-cells in the endocrine pancreas will be stimulated, and insulin in turn stimulates the uptake in the majority of body tissues of glucose from blood by increasing the number of active glucose transporters, GLUT4 at the cell membrane. In addition, insulin inhibits hepatic gluconeogenesis and glycogenolysis, and thereby the output of glucose from the liver.

The mammary gland takes up glucose by a different and non-insulin dependent glucose transporter, GLUT1. As shown in Table 17.6, GLUT 1 has a lower Km value than GLUT4 allowing the mammary gland to efficiently extract glucose even when plasma concentrations are very low. In this way, insulin becomes a factor that can determine the relative partitioning of glucose between mammary and non-mammary tissues, and when insulin concentrations are low, glucose will be partitioned in favour of the mammary gland.

Onset of lactation is associated with a dramatic increase in uptake of glucose, amino acids and lipids by the mammary gland. In dairy cows, plasma glucose and insulin are reduced immediately after calving associated with the onset of copious milk secretion, and this triggers mobilization of particularly body fat and results in negative energy balance early in lactation [54]. However, studies have shown that glucose (Figure 17.13A) is not decreased right after parturition in the sow, but merely increases after parturition and only gradually decreases after the sow has been lactating for 1-2 weeks. This is likely a consequence of the gradual increase in both milk production and the associated mammary glucose consumption in the sow with progress of lactation.

Glucose is the most important factor stimulating insulin secretion from the pancreas. However, neither preprandial nor postprandial insulin concentrations decreased along with plasma glucose levels 2-4 weeks after parturition (Figure 17.13C) when glucose concentrations were lowest. Postprandial insulin concentrations were in fact higher during lactation than during gestation. Some of the blood that is drained from the viscera (i.e. enriched with nutrients absorbed from the gastrointestinal tract) passes the pancreas before it enters the portal vein and reaches the liver, and this allows the pancreas to detect and respond to glucose absorption. Therefore, the postprandial insulin response must reflect a direct response of the pancreas to glucose concentrations in venous blood drained from the viscera. Postprandial insulin levels thus follow the rise in feed intake (and glucose absorption) over the first weeks of lactation.

Glucose absorbed from the gastrointestinal tract is high in monogastric animals, including the pig, and the glucose delivery to the liver increases with feed intake in early lactation. In addition, the milk yield of sows during the first days after onset of lactation is much lower for sows than for dairy cows, and these differences may be the main explanations why sows, in contrast to ruminants, only rarely develop ketosis around parturition. The liver of the sow does not have the extra metabolic stress associated with gluconeogenesis from oxaloacetate, and since this is an intermediate in the citric acid cycle, gluconeogenesis in ruminant animals can interfere with the capacity of the citric acid cycle to oxidise acetyl-CoA units generated during β-oxidation of fatty acids, resulting in their redirection into formation of ketone bodies [2].

There is, however, no reason to believe that sows should not develop fatty liver, although it likely will occur later in lactation when the metabolic load is at its maximum. It has not been possible to find any studies addressing this issue in sows. Fatty livers develop as a consequence of an imbalance between fatty acid uptake and incorporation into TAG relative to the capacity of the liver to export these TAG incorporated into very low density lipoproteins (VLDL). It has been shown in in vitro studies by Emery et al. [18] that the liver of pigs possesses the ability to increase the uptake and incorporation of fatty acids into TAG in response to increasing concentrations in the media just as cattle, and they have the same limited ability to export TAG, rendering them vulnerable to accumulation of TAG when plasma concentrations of NEFA are high. From Figure 17.13B, it is evident that the sow must be faced with this challenge, not immediately postpartum, but after the first 1-2 weeks of lactation when NEFA levels in plasma increase to very high levels, which in some sows become as high as 2mM prior to feeding [44].

The puzzling question at this point is why the sow is mobilising body fat and protein at all during lactation, and ends up having these high levels of NEFA in plasma, when the anabolic hormones insulin (postprandial) and IGF-1 (see below) are increased during lactation relative to gestation, which should favour protein and fat deposition and prevent release of NEFA from adipose tissue?

There is no precise answer to this question, but the decrease in plasma glucose (Figure 17.6A; due to mammary consumption) is expected to have negative impact on glucose uptake by the GLUT4 transporter, as normal plasma concentrations are close to Km values for this transporter, and uptake is most sensitive to changes when plasma concentrations are close to the Km value. Preprandial concentrations as low as 1.7-2.2 mM have been reported in lactating sows [44], which is less than 50% of the Km value. The same may apply to amino acids (Figure 17.13G). In addition, early lactating sows develop insulin resistance as also observed in ruminants, and thus higher insulin concentrations are required to stimulate a given glucose uptake, which obviously will favour the mammary gland in the competition for the key nutrients glucose and amino acids, and can alter the balance in adipose tissue metabolism towards a more catabolic state.

8.2. Glucagon

Like insulin, this hormone is a peptide. It exists in two forms of which one, pancreatic glucagon, is secreted from α-cells in the endocrine pancreas and the other, gut glucagon is secreted from the intestinal mucosa. The secretion is stimulated by low plasma glucose concentration, and by amino acids, SCFA and the gut hormone CCK, the secretion of which is enhanced by increased protein flow to the small intestine. The major effects of glucagon are stimulation of hepatic gluconeogenesis and glycogenolysis, i.e. increase of glucose output from the liver (see [45]. Glucagon may also have some acute effect on lipolysis by stimulation of hormone sensitive lipase in adipose tissue [66], but it is questionable whether this has any major significance in the regulation of nutrient partitioning between extra-hepatic tissues. The main function of glucagon is thus its important role (antagonistic to insulin) in the regulation of endogenous glucose production. This is of major importance for adaptation to lactation in ruminants. It is not known if glucagon has any major importance for adaptation to lactation in sows that on normal diets to a large extent presumably are able to satisfy their requirements for glucose via absorption from the gastrointestinal tract.

8.3. Triiodothyronine (T_3) and thyroxine (T_4)

These hormones are synthesized in the thyroid gland from the amino acid tyrosine and iodine. The secretion from thyroidea is regulated by a feedback system in which thyrotropin-releasing hormone (TRH) from hypothalamus stimulates secretion from the anterior pituitary of thyroid-stimulating hormone (TSH = thyrotropin), which in turn enhances the secretion of the thyroid hormones. T_3 and T_4 in turn have inhibitory effect on secretion of TRH and TSH at both the hypothalamic and the pituitary levels, which constitutes a negative feedback control system. The blood plasma concentrations of T_3 and T_4 are affected by energy balance and by body temperature. The energy balance is positively related and the body temperature is negatively related to the level of the thyroid hormones [72], [5]. Generally, T_3 and T_4 stimulate metabolic rates and thereby the use of energy and heat generation in target tissues, with the mammary gland as an important exception as it does not appear to express receptors for thyroid hormones. T_4 is present at much higher plasma concentrations than T_3, which is the biologically most active form. T_4 is activated to T_3 by means of deiodinases in the target tissues. Some interaction exists between the thyroid hormones and somatotropin (ST) as ST stimulates the activity of deiodinases and thereby also the effect of the thyroid hormones. On the other hand, T_3 enhances the effect of ST by increased synthesis of ST receptors (at least in the liver) and thereby has an indirect endocrine effect via IGF-1 [75].

The generally stimulating effect of the thyroid hormones on tissue metabolism contributes to facilitate enhanced nutrient retention and growth as high turnover rates are positively related to high growth rates [72]. However, the stimulating effect on the anabolic processes depends on adequate nutrient supply, which is not the case for the stimulating effect on the catabolic processes. This means that in a situation in which T_3 and T_4 plasma levels were increased without concomitantly increased nutrient supply, catabolism would prevail and alter the balance of protein and lipid metabolism in non-mammary tissues towards mobilization.

In a study by Giesemann et al. [25], T_3 and T_4 plasma levels were observed to decrease during the last four weeks of gestation in primiparous sows, and increase within one week after farrowing and remain at this level throughout the rest of the lactation period. This pattern also contrasts

observations among ruminants where T_3 and T_4 drop dramatically at the onset of lactation [73]. It was also observed that a high-energy diet, as expected, increased plasma levels of T_3 and T_4, and on this diet the time to first oestrus was also shorter. However, this could not be related to thyroid hormones since exogenous administration of a thyroxine secretagogue had no effect on days to first oestrus [25]. The precise role of thyroid hormones in the homeorhetic adaptation to lactation in the sow therefore remains to be established.

8.4. Somatotropin (growth hormone) and insulin-like growth factor-1

Somatotropin (ST) and insulin-like growth factor-1 (IGF-1) are both peptide hormones. They are described together because ST controls secretion of IGF-1, and IGF-1 exerts most of the growth-stimulating effects of ST. ST is secreted from the anterior pituitary, and secretion is regulated by superior hormones from the hypothalamus: growth hormone-releasing hormone (GRH), which enhances, and somatostatin, which inhibits the secretion of ST. IGF-1 also controls ST secretion by a negative feedback system directly on ST release from the pituitary, and indirectly by stimulating the release of somatostatin from hypothalamus.

The endocrine IGF-1 circulating in blood originates mainly from the liver. Secretion is stimulated upon binding of ST to high affinity receptors on the hepatocytes. ST can also stimulate paracrine synthesis of IGF-1 in most animal tissues, with the ovary as an important exception. Both high and low affinity receptors have been identified in the liver [26], but only binding to the high affinity receptor is coupled to secretion of IGF-1. Insulin stimulates the synthesis of high-affinity receptors for ST in the liver. Therefore, in situations with low insulin concentration, uncoupling of the ST-IGF-1 axis will occur, where binding of ST to liver cells are down regulated and the IGF-1 synthesis and release from the liver are reduced. This in turn means less inhibition of ST secretion from the pituitary and the result is a situation with high ST and low IGF-1 levels. This is characteristic of the dairy cow in early lactation, but it is quite evident from patterns of changes in ST (Figure 17.13D) and IGF-1 (Figure 17.3E) that a similar uncoupling of the ST-IGF-1 axis does not occur in sows in early lactation, and insulin is once again the key factor responsible for the species differences. Insulin is not reduced during lactation, ie. functional high-affinity receptor are present in the liver capable of responding to changes in plasma ST concentrations, and IGF-1 therefore increases in response to increases in ST after farrowing in the sow. Nonetheless, sows that become catabolic during lactation will have reduced IGF-I concentrations [53]. The reason for the increase in ST after farrowing can be ascribed to suckling, as this is known to be a potent stimulator of ST in sows, and hence ST secretory patterns are sensitive to changes in suckling intensity [44]. Therefore patterns of change in ST and prolactin (Figure 17.13F) in the sow are very similar across the lactation period.

8.5. Somatotropin

It is widely accepted that most growth promoting effects of ST are mediated by IGF-1. This also includes effects in the mammary gland as receptors have never been demonstrated for ST in this organ. ST is known to stimulate milk production in cows via IGF-1 (see below). A galactopietic effect of ST in the sow has also been demonstrated [33], but in most studies ST treatment had no effect on milk production (e.g. [15], [86]). In this context, it should be remembered that ST treatment responses in dairy cows most often have been negligible when treatment was administered before peak lactation [20]. ST treatment in all studies with sows were concluded at peak lactation, and treatment effects, if any, were observed only in the last 1-2 weeks before weaning [33].

The major direct metabolic effects of ST are targeted at adipose tissues and muscle (Table 17.13). In adipose tissues ST stimulates lipolysis and decreases lipogenesis as a result of a marked reduction in sensitivity to insulin as well as decreased activity of lipoprotein lipase (LPL) and acetyl-CoA carboxylase [6], [49], [9]. Furthermore, ST stimulates the lipolytic effect of catecholamines most likely by downregulation of α-receptors and in turn the inhibiting effect of adenosine on hormone sensitive lipase (HSL) [49]. In muscle tissue, ST stimulates protein turnover and protein retention provided that the energy and especially the amino acid supply is adequate [57]. Evidence also suggests that ST also can stimulate satellite cell proliferation and fusion, which are processes essential for growth and repair of skeletal muscle fibres [76]. It is still uncertain, however, how

much of the anabolic effect in muscle is due to direct actions of ST or how much is mediated via paracrine IGF-1 (see later).

Hence, increased ST concentration in the blood at the onset of lactation (Figure 17.13D) will directly act to increase NEFA release and decrease TAG uptake in adipose tissue, decrease glucose uptake in muscle and adipose tissues, and hence increase nutrient supply to the mammary gland. These direct effects of ST are likely to play an important role in the homeorhetic adaptation to lactation in sows, and can contribute to explain the paradoxical observations that a negative energy balance and high blood concentrations of NEFA can be induced in sows during lactation despite higher circulating levels in blood of the two anabolic hormones, insulin and IGF-1.

8.6. IGF-1

IGF-1 mediates most of the anabolic effects of ST. Most of the circulating IGF-1 is attached to specific IGF-1 binding proteins (IGFBP), all of which have higher affinity for IGF-1 than do tissue receptors [14]. The high affinity of the binding proteins is reflected in the half-lives ($T_{½}$) of IGF-1 and the IGFBP complexes. $T_{½}$ of free IGF-1 is in the order of 3-4 minutes, but is 45-60 minutes and 14 hours for IGFBP1/IGFBP2 and IGFBP3 complexes, respectively [36], [17]. As the biological effects of IGF-1 depend on its binding to receptors in target tissues, the distribution of IGF-1 among the different BPs and the ability of the tissues to free IGF-1 from its binding proteins are important factors to determine the biological effect of IGF-1.

Effects of ST on the mammary gland are assumed to be mediated by IGF-1. IGF-1 is a potent mitogen for mammary epithelial cells and a potent inhibitor of apoptosis (programmed cell death) [14]. It has been shown that IGF-1 increases the m-RNA content in mammary epithelial cells and the capacity for protein synthesis in ruminants [6]. In addition to this, high blood plasma levels of IGF-1 increase the blood flow to the udder [69], [59], which can be attributed partly to a direct vasodilation effect and partly to an indirect effect of high metabolic activity in the mammary tissue. Whether IGF-1 has similar effects in the sow mammary gland is not clear, but increasing levels of IGF-1 in the sow in early lactation could in that case contribute to stimulate mammary development and lactation performance.

In muscle tissue, IGF-1 stimulates protein synthesis and cell proliferation in satellite cells, and can both be the result of endocrine or paracrine communication stimulated by ST [57]. IGF-1 is the only hormone known to stimulate cell division in chondrocytes in the epiphyseal plates, i.e. the growth zones in long bones [19]. Hence, IGF-1 has an essential, although indirect effect, on muscle growth by stimulating longitudinal bone growth in young individuals [77]. IGF-1 is also known to stimulate adipose tissue development and growth early in life [57] and presumably also later in life. Overall, the nutrient partitioning among body tissues is changed in favour of muscle protein retention by ST because of its direct and IGF-1 stimulated growth promoting effects on muscle and catabolic actions in adipose tissues. This is the reason why in some countries exogenous ST is used as a growth promoter in meat producing animals.

As discussed above, it is paradoxical that energy balance becomes gradually more negative in sows over the first weeks of lactation, when the two anabolic hormones insulin and IGF-1 are substantially increased over the same period. It is not known if IGF-1 sensitivity in non-mammary tissues is decreased as for insulin during early lactation.

Sows that are nutritionally compromised will, however, have reduced concentrations of insulin and IGF-I in their blood. This may not have significant impact on the metabolic adaptation to lactation and performance of the sow during lactation as such, but it can theoretically reduce ovarian responsiveness to gonadotropins, and thereby contribute to explain carry-over effects from sow performance during lactation and impaired development of the ovarian follicular population after weaning [53].

8.7. Leptin

A defect in the ob (obese) gene, which encodes for leptin, leads to inefficient appetite regulation, decreased metabolic rates, development of obesity, prevention of puberty and normal oestrus cycle in mice [1]. Leptin is therefore considered as an anti obesity hormone and an important factor linking nutrition and reproductive function. Due to analytical challenges with assays for leptin, most of the present knowledge on physiological effects of leptin therefore originates from studies in rodents and humans, and should be taken cautiously when related to other species. However, leptin is likely to play an important role also in the adaptation of sow metabolism to low nutritional/metabolic states, where it is involved in regulation of both appetite and energy expenditure in the body.

Leptin is produced predominantly in white adipose tissue, but the leptin gene is also expressed in placental and foetal tissues as well as in mammary and other tissues, where paracrine leptin synthesis can take place. Leptin receptors have been identified in several tissues, e.g. hypothalamus, anterior pituitary, white adipose tissue and mammary tissue, and the hypothalamus and pituitary in the brain seem to be important target organs for leptin, which can pass the blood-brain barrier from the circulation by a specific transport mechanism.

Fat is mobilized from adipose tissue during lactation when the sow is in negative energy balance as described previously. As a consequence, the size of adipocytes and synthesis and secretion of leptin are reduced, explaining the decreased leptin levels during lactation (Figure 17.13H). The decreased binding of leptin to specific receptors on hypothalamic neurones will increase the synthesis of two neuropeptides (neuropeptide Y = NPY and Agouti-related peptide = AGRP), which are potent stimulators of appetite. At the same time, synthesis of two other factors (pro-opiomelanocortin = POMC and cocaine- and amphetamine-related transcript = CART) are downregulated. These factors have powerful inhibiting effects on appetite [1]. This supports the theory of a mechanism for lipostatic regulation of feed intake, i.e. how the organism seeks to maintain a relatively constant fat content by adjusting energy intake according to energy expenditure. In agreement with the role of leptin as a satiety factor, sows fed a high-fibre diet during gestation were shown by Quesnel et al. [70] to have lower carcass fat contents at farrowing and consequently lower circulating leptin levels, and this allowed for increased appetite during lactation.

Leptin also affects the synthesis of a number of releasing hormones in hypothalamus. Low binding of leptin to hypothalamic receptors elicits the following reactions: enhanced and reduced synthesis of somatostatin and GRH, respectively, decreased synthesis of TRH and increased synthesis of corticotropin-releasing hormone (CRH). The ensuing responses at the pituitary level cause blood plasma concentrations of somatotropin and IGF-1 (see next section) and thyroid hormones to decrease during feed deprivation.

Reduced leptin binding in hypothalamus also decreases the synthesis of gonadotropin-releasing hormone (GnRH), which controls the synthesis of the two sex hormones, the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH) in the anterior pituitary. This could explain the well-known relationship between body condition, i.e. fatness, and time of puberty, and it may also explain incidents of anoestrus or poor reproductive performance in the next lactation in sows experiencing extensive weight loss during lactation. Reproduction is, however, not the topic of this chapter.

The most well-known peripheral actions of leptin are reduced tissue sensitivity to insulin, leading to decreased lipogenesis and enhanced lipolysis in adipose tissue as well as increased fatty acid oxidation in muscles. These are anti-insulin effects resulting in repartitioning of the lipid metabolism. However, the physiological importance of these effects in lean animals is uncertain.

9. Quantification of protein and energy metabolism of lactating sows

As described earlier, the lactation period is associated with a massive excretion of nutrients via the milk. Quantitative studies on protein and energy metabolism can be performed at animal level using balance studies, i.e. total collection of faeces and urine for a period over several days and measurements of milk production using the D_2O dilution technique. A quantitative study on nitrogen (protein) metabolism showed that sows in weeks 2, 3 and 4 after parturition secreted 44, 51 and 52% of ingested nitrogen via milk [79]. Thus during the last three weeks of lactation, an average of 49% of ingested nitrogen ended up being secreted as protein in the milk (Figure 17.14 left). Concomitantly, the average loss of nitrogen via faeces was 17% and the loss in urine amounted to 29% of ingested nitrogen. The nitrogen balance, which is the difference between intake and output of nitrogen in milk, faeces and urine, was estimated at 5% of ingested nitrogen, which suggests that sows are retaining minor amounts of protein during peak lactation. However, the nitrogen balance was overestimated due to evaporative loss of ammonia from the urine, and based on the weight loss of the sows, the nitrogen balance was likely slightly negative.

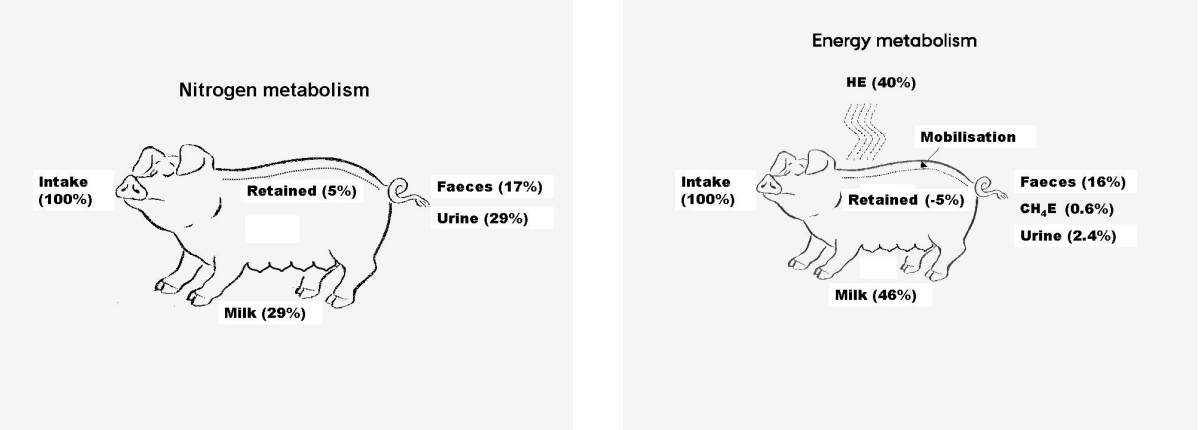


Figure 17.14. Metabolism of dietary nitrogen (left) and dietary energy (right) of lactating sows at peak leactation.

In the study described above, the utilisation of dietary energy was also quantified. Relative to the amount of energy supplied via the feed (100%), an average of 46% of the energy was secreted via the milk (Figure 17.14 right). In the study, the secretion of energy increased from 41% in week 2 to 48 and 49% in weeks 3 and 4, respectively, which was associated with increased milk production as lactation progressed. During the entire period, averagely 40% was lost as heat; 16% in faeces; and 3% lost via urine and gases. The study did also allow separation of the heat production into which nutrients were being oxidised, and, on average, oxidation of carbohydrates, protein and fat contributed with 82, 13 and 5% of the heat produced. The energy balance, i.e. the difference between intake and energy consumption, was estimated at -5% of ingested energy, which reveals that lactating sows are mobilising energy from the body. The sows lost weight during the study and calculations revealed that the sows mobilised energy from both fat and muscle tissues, which emphasised that the positive protein balance described above indeed was overestimated. In the study, one group of sows was fed a high-fat diet to evaluate whether supplementation of 8% animal fat to the diet would affect the milk yield or the energy balance of the sows, but no significant effects were found on these traits. However, addition of 8% dietary fat reduced the amount of de novo synthesized fat for milk synthesis from 364 to 117 g/day [79].

10. Performance of piglets

In the literature, major attention has been paid to production parameters like number of liveborn and stillborn piglets, piglet survival and litter weight gain due to the feasibility of data recording. In contrast, intake of colostrum and milk of suckling piglets (along with mobilization of nutrients in sows) are seldom quantified, even though these traits directly affect performance of the piglets (survival and growth) and performance of the sows.

10.1. Piglet mortality

Mortality of newborn piglets peaks during the first 1-2 days of life, and most deaths are caused by inadequate amounts of energy stored in the body or inadequate intake of colostrum/milk [67], [21]. The perinatal period is associated with abrupt changes in energy supply from that supplied in maternal blood via the umbilical cord to that supplied by colostrum and milk via mammary gland secretions. Newborn piglets have no or limited capacity/capability to oxidise body protein and body fat [55], and therefore piglets are dependent on energy from three different sources: glycogen, colostrum and milk (Figure 17.15). Initially, piglets rely on body energy reserves, and the glycogen depots at birth are sufficient to support normal activity for around 16 hours [83]. Shortly after birth (typically within 20-30 minutes), the piglets start to suckle colostrum, and oxidation of ingested lactose and fat from colostrum replace to some extent oxidation of glycogen. After around 12 hours, the amount of colostrum available for piglets becomes limited and piglet rate of gain levels off until milk production is initiated around 32-33 hours after farrowing was initiated (Figure 17.2).

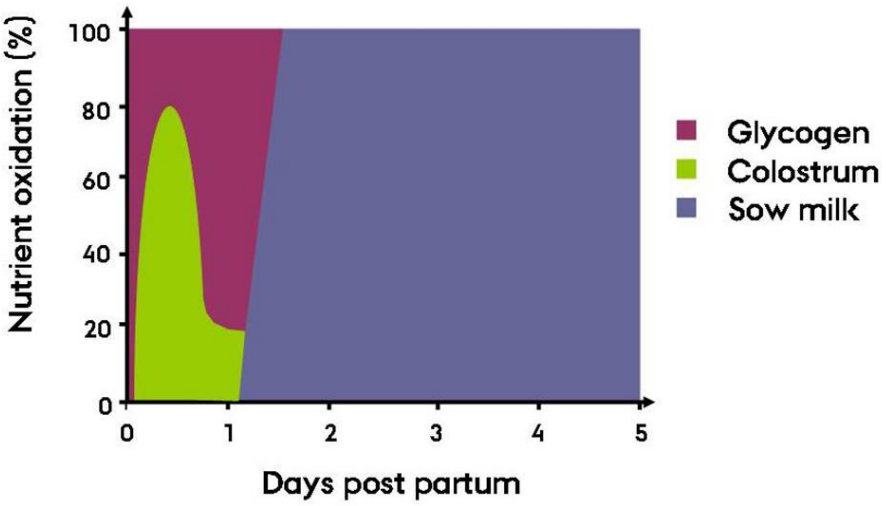


Figure 17.15. Oxidation of nutrients in piglets (in % of their heat production) during the first critical days postpartum).

At birth, the piglet liver is literally loaded with glycogen, because half of the liver mass can be ascribed to stored glycogen (10% glycogen + 40% retained water associated with glycogen deposition on a wet weight basis). The glycogen pools are being build-up in the fetuses during the last month of gestation, and several attempts have been made to improve these pools by focusing on the nutrient supply for late-gestating sows, mainly feeding strategy or feed composition. It is possible to affect the glycogen pools slightly depending on the experimental conditions (and sow nutrition), but normally sow nutrition in late gestation is not a limiting factor for glycogen retention in foetuses.

Colostrum is important for neonatal survival for two reasons. Firstly, colostrum is essential as an energy source until milk secretion from the mammary gland becomes copious around 32 hours after first piglet is born [46]. Secondly, colostrum is loaded with antibodies against infections and diseases experienced by the sow, and the antibodies supply piglets with passive immune de-

fence, which is important for piglet survival and performance throughout the suckling period and even after weaning. In a recent study, it was demonstrated that colostrum intake of piglets may be enhanced by altered dietary supply to sows during transition [31]. The study showed that medium-chain fatty acids in the maternal diet and short-chain fatty acids in sow plasma (originating from fibre fermentation) were beneficial factors for the colostrum intake, whereas long-chain fatty acids from the diets inhibited the colostrum intake. Furthermore, piglets with a high colostrum intake had a higher survival rate 0-24 hours after birth.

The major determinant of neonatal death is the live weight of the neonate piglet. When piglets are born with a live weight below 1400 g, mortality rates increase and become progressively higher with decreasing live weight [85]. Piglets weighing less than 800 g at birth have a very poor chance of surviving. There are several reasons for that. First of all, smaller piglets have higher heat loss due to a high surface-to-volume ratio, i.e. they are less resistant to cooling. Secondly, their glycogen pools in liver and muscles are much smaller, simply because the mass of these organs are smaller. Thirdly, piglets with a low live weight have a smaller gastric capacity and ingest less colostrum. And fourthly, the small piglets are typically weaker (less vigorous) and have problems in getting access to a mammary gland especially in large litters.

The mortality of piglets is primarily associated with hunger or crushing. Indeed, many neonatal deaths are said to be caused by crushing, but they typically occur in response to inadequate intake of colostrum or milk. A low milk intake makes the piglet unable to intercept the signals when the sow wants to change posture from standing to lying. Piglets may also die of diarrhoea or other infections/diseases, and in that respect, the immune defence obtained from immunoglobulins in colostrum is crucial.

10.2. Piglet growth and conversion of milk

Piglet birth weight averages approx. 1.50 kg and weaning weight (at 28 days of age) around 7.5 kg. On average, suckling piglets grow approx. 220 g/day. Growth of individual piglets can be described as a linear function of the age, except for the first two days (Figure 17.15). However, some piglets grow much faster (> 300 g/d) and some grow quite slowly (less than 150 g/d). As a corollary, the variation of weight within a litter increases with age (Figure 17.16). The milk intake of piglets increase with their age until peak lactation in week three or four, but so does the amount of milk required for maintaining a constant live weight. A previous study found that piglets required 317, 517 and 582 g/day to maintain their live weight on days 4, 11 and 18, respectively [78]. Thus, the larger the piglet, the more milk is required to support body growth, and these relationships also indicate that there is not a constant conversion factor that can be used to calculate milk intake from live weight gain.

Conversion of milk to piglet growth depends on the age of piglets, as described above, but it is also affected by the milk intake itself. The reason is that retention of protein in the piglet is prioritized higher than retention of fat [61]. Thus, piglets that have a high milk intake will respond by retaining considerable amounts of fat, but the extra weight gain due to fat retention is negligible compared to growth caused by protein retention, because retention of 1 g of protein is associated with 4.2 g retained water, whereas 1 g of retained fat only is associated with 0.15 g of retained water. As an average over a 4-week lactation period, 1 kg of piglet gain requires approximately 4 kg of milk produced by the sow, which corresponds to 0.7-0.8 kg dry matter secreted in milk. However, behind these figures, individual differences, stage of lactation and the actual milk intake greatly affect the conversion factor (gram milk per gram gain). As a consequence, the sow milk yield cannot accurately be estimated using litter (or piglet) weight at weaning. It is more precise to estimate the milk intake of individual piglets on selected days and then derive the milk yield of the sow by summing up the estimated intake of individual piglet within the litter.

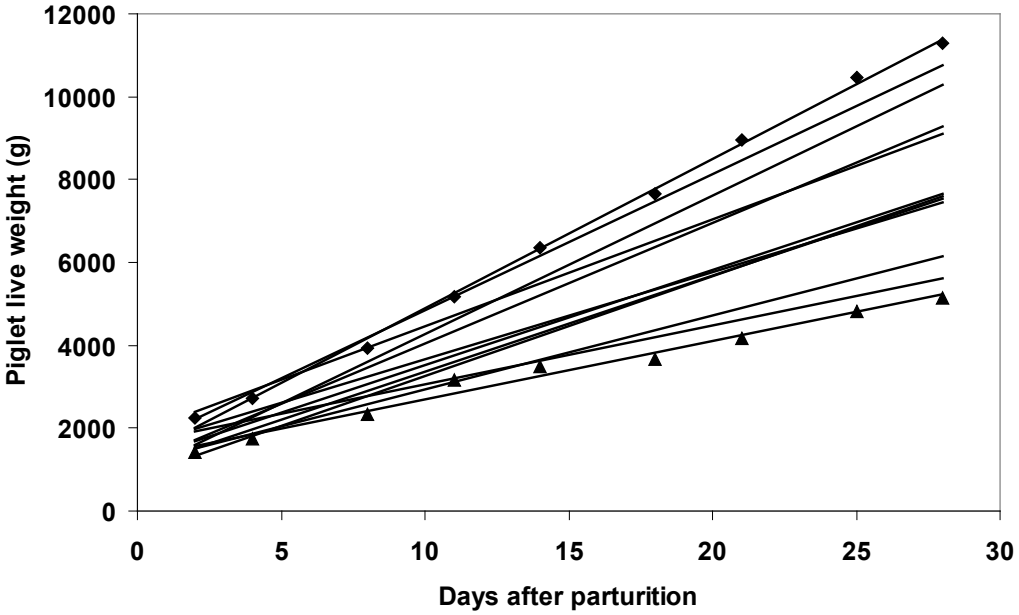


Figure 17.16. Variation of live weight within a litter increases with age, but growth of indivudal piglets may be described as a linear function from day 2 until weaning at day 28. The growth rate of the heaviest (diamond) and the lightest piglets (triangle) was 334 and 138 g/day, respectively.

10.3. Chemical composition and nutrient retention of suckling piglets

The carcass of newborn piglets consist mainly of water (79%), protein (12.1%), minerals (4.4%) and an impressingly high amount of glycogen stored in liver and muscle tissues (2.8%) , whereas the body contains only minor amounts of body fat (1.1%). In a French study with suckling piglets, the nutrient retention and metabolic rate were quantified from birth until day 22 of lactation [61]. They reported that on average, suckling piglets retained considerable amounts of protein and fat (averagely 28 g protein and 27 g fat daily). They also demonstrated that piglets with a low milk intake retained relatively more protein and less fat compared with piglets with a high milk intake. The chemical composition of piglets changes considerably during the suckling period, and compared to piglets at birth, carcasses at weaning have a lower relative content of water (68%) and a lower content of ash (3%), a slightly higher relative content of protein (14.9%) and a considerably higher relative content of body fat (11.3%).

10.4. Nutrient supplements to suckling piglets

Nutrients may be supplemented to piglets either in the form of milk replacer or creep feed, depending on the age of the piglets. Early in the suckling period, piglets can be supplemented or fed solely with milk replacer if the sow is consuming inadequate amounts of milk. However, milk replacer is typically based on cow milk, which is less abundant in milk solids than sow milk. In addition, milk replacers are rather low in dietary fat compared to sow milk due to physical properties (it is difficult to solubilize fat in water). As a corollary, the supply of fat, and especially dietary energy, to the suckling piglet is rather low when fed milk replacer, and consequently, the piglets retain less amounts of body fat [82]. Consequently, piglets raised solely on milk replacer will have minor fat depots at weaning and be more vulnerable around weaning and less productive after weaning when high protein retention is driven partly by fat oxidation.

In weeks 3 and 4 of lactation, it is common in practical pig production to supply suckling piglets with dry feed on the floor. The intake of dry feed of piglets in this period is rather limited and amounts to 0.3 feed units per piglet until weaning [85] compared to approx. 200 feed units ingested by sows during a 4-week lactation period. Thus, the intake of dry feed of suckling piglets contributes with negligible amounts of metabolizable energy, but the dry feed is likely beneficial for the piglets in terms of adapting the gastrointestinal tract to solid feed before weaning.

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